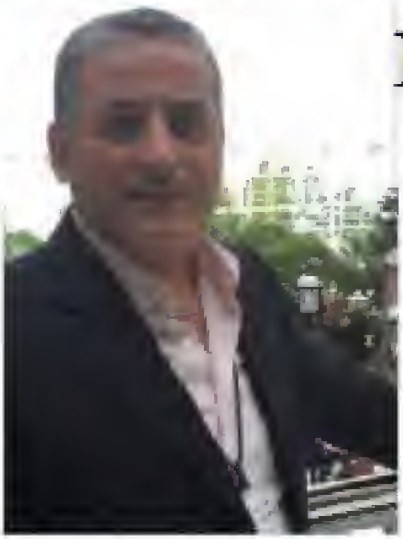
Illustrated Baby Nelson

General Pediatrics



Maryland USA 2017

By

Dr Mohamed El Koumi

Consultant pediatrics and pediatric nephrology
MD Pediatrics
Membership of Royal College of Pediatrics and Child Health (MRCPCH; UK)
IPNA Senior Clinical Fellow Pediatric Nephrology, Glasgow, Scotland (UK)
Assistant professor of pediatrics, Zagazig University

Address: Dr Mohamed El Koumi pediatric center- Abazia mall, Central corridor- 6 October City, Giza
Mobile: 00201000089045 Face book: Mohamed ElKoumi
E mail:Mohamed_197226@hotmail.com

اهداء

الى امى وابى ....اسالكم لهم الدعاء

الى زوجتى وابنائى واخى واخوتى

الى وجوه جميلة وارواح طاهرة تركتنا الى رحاب الله لازلنا نذكرها

الى اولئك الذين غمرونى بعلمهم وفضلهم.... اساتذتى وزملائى بمستشفى الاطفال الجامعى بكلية الطب جامعة الزقازيق

اقدم لكم كتابى

Contents

Growth and development

Factors affecting growth

1. **Prenatal factors**
   - Familial (genetic);children inherit their height pattern from their parents
   - Racial; some races are shorter than others e.g. Chinese
   - Constitutional
2. **Factors operating during pregnancy** (In Utero Exposures)
   - Maternal diseases e.g. diabetes mellitus, hypertension
   - Maternal exposures: Teratogens, infections e.g. TORCH, irradiations…
   - Maternal nutritional state.
3. **After birth**
   a. Age: Growth rate is more during infancy and adolescence.
   b. Sex:
      - Growth rate is nearly equal in males & females from birth till 11 years
      - Girls grow faster between 11 – 14 years (due to earlier puberty)
      - Boys grow faster than girls beyond 14 years (due to later puberty)
   c. Nutritional status → Chronic under nutrition & malnutrition retard growth
   d. Psychological and socioeconomic status
   e. Health status → chronic diseases retard growth
4. **Hormonal role**: growth is controlled by hormones depending on the stage

Intrauterine	Infancy & childhood	Adolescence
1. Chorionic gonadotropines 2. Placental lactogen 3. Insulin 4. Thyroxin (skeletal growth)	1. Thyroxin 2. Growth hormone	Sex hormones (Estrogen & androgen) are responsible for growth spurt during puberty

So

- Newborn of diabetic mother whose mother has hyperglycemia during pregnancy commonly have hyperinsulinemia and eventual macrosomia at birth
- Newborn with congenital hypothyroidism usually has delayed bone age screened for by plain radiograph on his knee that shows absent tibial and femoral epiphyseal centers that normally present at birth
- Newborn with growth hormone deficiency usually has normal size at birth simply because growth hormone actions operate after birth onwards

Assessment of Growth

I. Anthropometric measures

1. Weight

* At birth → 3 - 3.5 kg
* During the 1st year:
  - 1st 4 months → Weight ↑ by ¾ kg per month.
    So, weight at 4 months = 6 kg ⇒ double birth weight
  - Next 4 months → Weight ↑ by ½ kg per month
  - Last 4 months → Weight ↑ by ¾ kg per month.
    So, weight at 1 year = 9 kg ⇒ triple birth weight
* Beyond the 1st year → Weight is calculated as: **weight = age (in years) × 2 + 8**

Physiologic weight loss:

* Initial weight loss usually occur during the first 3-4 days of life
* The baby loses about 10% of his birth weight due to:
  - Scanty milk flow
  - Poor suckling capacity
  - Passage of meconium & urine
* This weight loss is usually regained by the 10th day of life

2. Length/Height

* At birth → 50 cm
* At 6 months → 68 cm
* At 1 year → 75 cm
* At 2 years → 87.5 cm
* After the 2nd year → **Height = age in years × 5 + 80**

How to measure?

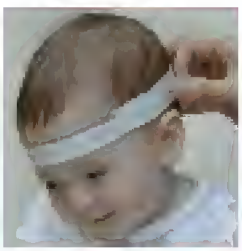
- Under 2 years: Length is measured in supine position
- Over 2 years: Height is measured in standing position

3. Occipto Frontal head circumference (OFC)

Clinical value

- OFC reflects the rate of brain growth.
- Maximum rate of brain growth & OFC is during the 1st year

* At birth → 35 cm.
* At 6 month → 43 cm
* At 1 year → 45 cm
* At 12 years → 55 cm



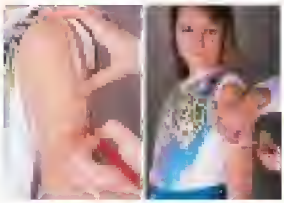
4. OFC & chest circumference (CC) ratio

Chest circumference is measured at level of xiphiod process in mid inspiration

Age	OFC/CC ratio
* At birth	> 1
* At 6 months	Equal 1
* at 1 year	< 1
* At 5th year	< 1

Clinical value: Suspect malnutrition if OFC/C.C > 1 beyond 6 months

5. Mid arm circumference (MAC)



* In a baby 1- 4 years → MAC is > 14 cm
* In border line malnutrition → MAC is 12 – 14 cm
* In severe malnutrition → MAC is < 12.5 cm

Clinical value

- Early indicator of malnutrition; and is not affected by edema.
- Often used for screening for malnutrition in lieu of weight for height
- MUAC divided by OFC classifies malnutrition into; Mild < 0.31 , moderate <0.28 , and severe < 0.25 (*Kanawati classification of malnutrition*)

6. Skin fold thickness

Clinical value: Estimate total body fat;

* Measured by skin fold calipers
* Measured at left triceps or left subscapular regions
* Normal values: - 10 mm at 1 year
  - 14 mm at 1- 4 years

8. The Arm span - Height relationship

* Span is shorter than height by 3 cm at 1-7 years.
* Span equals height at 8-12 years.

7. Proportions of upper segment & lower segment

* Upper segment (US) is measured from crown to symphysis pubis.
* Lower segment (LS) is measured from symphysis pubis to the floor.
* Proportions of US/LS:
  - At birth → 1.7 /1
  - At 3 years → 1.3 /1
  - After 7 years → 1 /1

Clinical value: Help evaluation of short stature

II. Teething

Primary = Deciduous or Milky teeth		Secondary (permanent) Teeth	
Tooth	Age (months)	Tooth	Age (years)
- Central incisor	6 - 9	- Central incisor	7
- Lateral incisor	9 - 12	- Lateral incisor	8
- 1st molar	12- 18	- Canine	10
- Canine	18- 24	- 1st premolar	11
- 2nd molar	24	- 2nd premolar	12
		- **1st molar**	**6**
		- 2nd molar	13
		- Wisdom tooth	22
* Count : 20 teeth * Teething starts at 6- 9 months and completed at 24 months. * The lower jaw incisors precedes the upper jaw by one month		* Count : 32 teeth * Teething start at the 6th years and completed at 22nd years * Eruption follow exfoliation immediate or may lag 4-5 months	

Teething Eruption Abnormalities

1. **Delayed teething**: No eruption beyond 13 months of age.

   Causes :

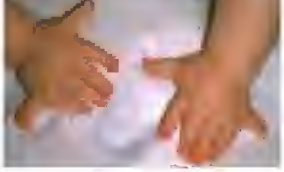
   a. Idiopathic : the commonest cause

   b. Local: e.g. supernumerary tooth, cysts, rigid gums

   c. Generalized: (DACRO H2); Down syndrome, Achondroplasia, Congenital hypothyroidism, Rickets, Osteogenesis imperfecta, Hypopituitarism, Hypoparathyriodism

2. **Premature teething** is seen is:

   - Natal teeth (should be extracted to avoid aspiration).
   - Congenital syphilis
   - Ellis Van Creveld syndrome:
     - Disproportionate dwarfism (short stature with short limbs)
     - Post axial polydactyly
     - Ectodermal dysplasia(teeth and nail)
     - Congenital heart disease (ASD)
     - Narrow chest



3. **Congenital missing or extra tooth**

III. Fontanels

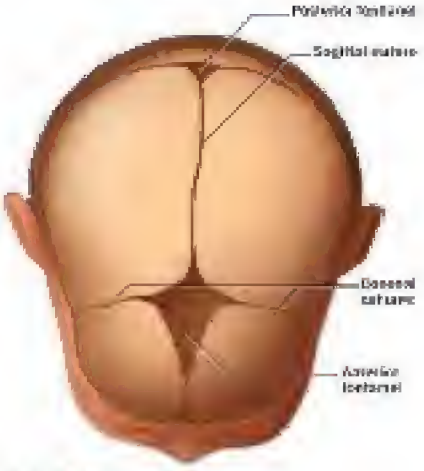
Posterior fontanel

÷ Normally: Closed at birth or opened < 0.5 cm and closes within 2 months

÷ Abnormally: Opened > 1 cm or Not closed within 4 months

Causes :

- Prematurity
- Increased intra cranial tension
- Mongolism
- Cretinism

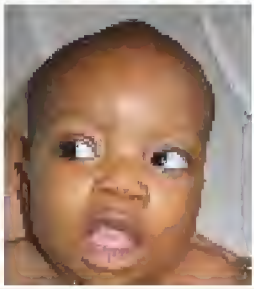


Anterior fontanel: Clinical value

1. Assessment of growth
   - At birth → 3 fingers (≈ 3- 4 cm).
   - At 6 months → 2 fingers.
   - At 12 months → 1 finger.
   - At 18 months → closed.
2. Size
   A- Large fontanel (delayed closure) in: (DACRO HI)
   - Down syndrome
   - Achondroplasia
   - Congenital hypothyriodism
   - Rickets
   - Osteogenesis imperfecta
   - Hypopituitarism
   - Increased intra cranial tension

   B- Small fontanel (premature closure; before 6 months) in: (2 C)
   - Craniosynostosis
   - Congenital hyperthyroidism
3. Surface : Normally it is smooth & continuous with the skull bones.

   A- Bulging: with ↑ intra cranial tension e.g.
   - Intra cranial infections
   - Hydrocephalus
   - Intra cranial hemorrhage



B- Depressed : in dehydration

IV. Osseous Growth

Normally; there are 5 secondary ossific centers at birth in

- Lower end of femur.
- Upper end of tibia.
- Calcaneus, talus & cuboid

"X ray knee in newborn help assess intrauterine skeletal maturation ; it is a good screening tool for congenital hypothyroidism"

Carpal bones start ossification after birth as follow

- The 1st carpal bone → ossifies at about 2nd month of age.
- The 2nd carpal bone → ossifies by the end of the first year.
- Later on, one carpal bone ossifies approximately each year till the 6th year; the 8th bone usually ossifies at the 12th year of age.

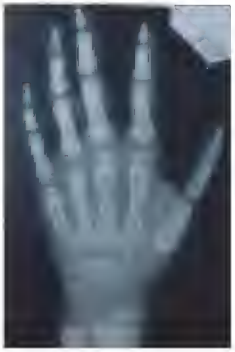
Bone age

- Bone age is a measure of the degree of skeletal maturity of a child
- It is measured in years by the radiographic examination of ossification centers; most often using the Greulich-Pyle bone age scale
  - At > 6 month onwards → by x-ray over the left wrist
  - In late childhood → by assessing fusion of epiphysis

Causes of Delayed Bone Age	Causes of Advanced Bone Age
1- Hypothyroidism	1- Hyperthyriodism
2- Hypopituitarism	2- Hyper pituitarism
3- Delayed puberty.	3- Androgen excess (e.g. congenital adrenal hyperplasia)
4- Cushing syndrome	4- Simple obesity.
5- Chronic illness / under nutrition	

Example for bone age estimation by *Greulich-Pyle* bone age scale

Average bone age 1 year



Average bone age 2 years

Average bone age 3 years

V. Growth Charts (Curves)

Values

1- Assess growth and normal growth variations among children
2- Early predictor of malnutrition (flattening of weight curve)
3- Monitor success of treatment of malnutrition

Examples

1. Percentile growth curves

Each chart is composed of 7 curves

- 97th percentile → Highest normal.
- 90th percentile → High normal.
- 75th percentile → Above average.
- 50th percentile → Average.
- 25th percentile → Below average.
- 10th percentile → Low normal.
- 3rd percentile → Lowest normal.

Normal child on percentile curves

- Should lie between the 3rd & 97th percentile curves. So, values < 3rd or above 97th are abnormal.
- On serial measurement deviation of the child from his own percentile curve is abnormal.
- Not all the child growth parameters necessarily fall into the same percentile.

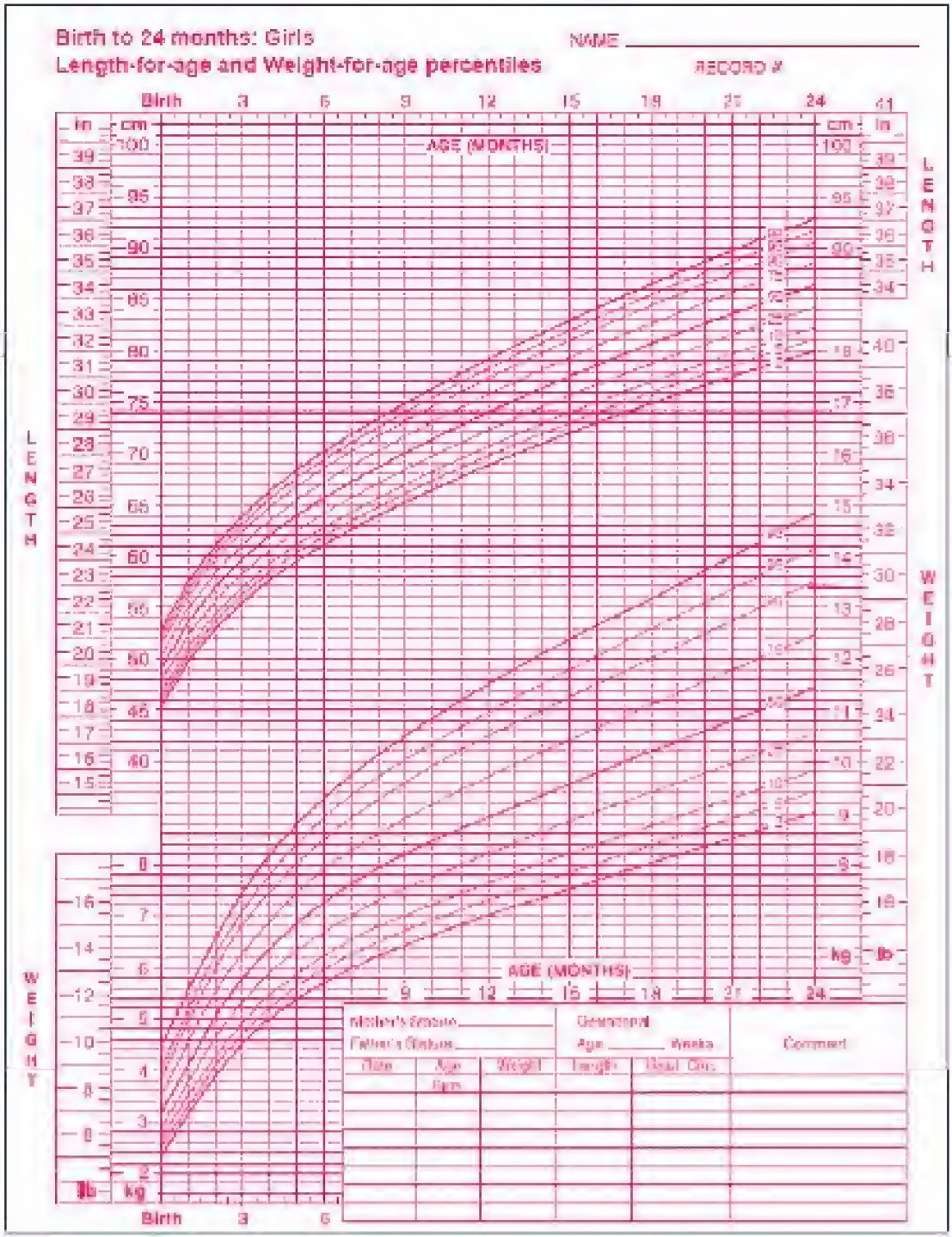
2. Growth velocity curves

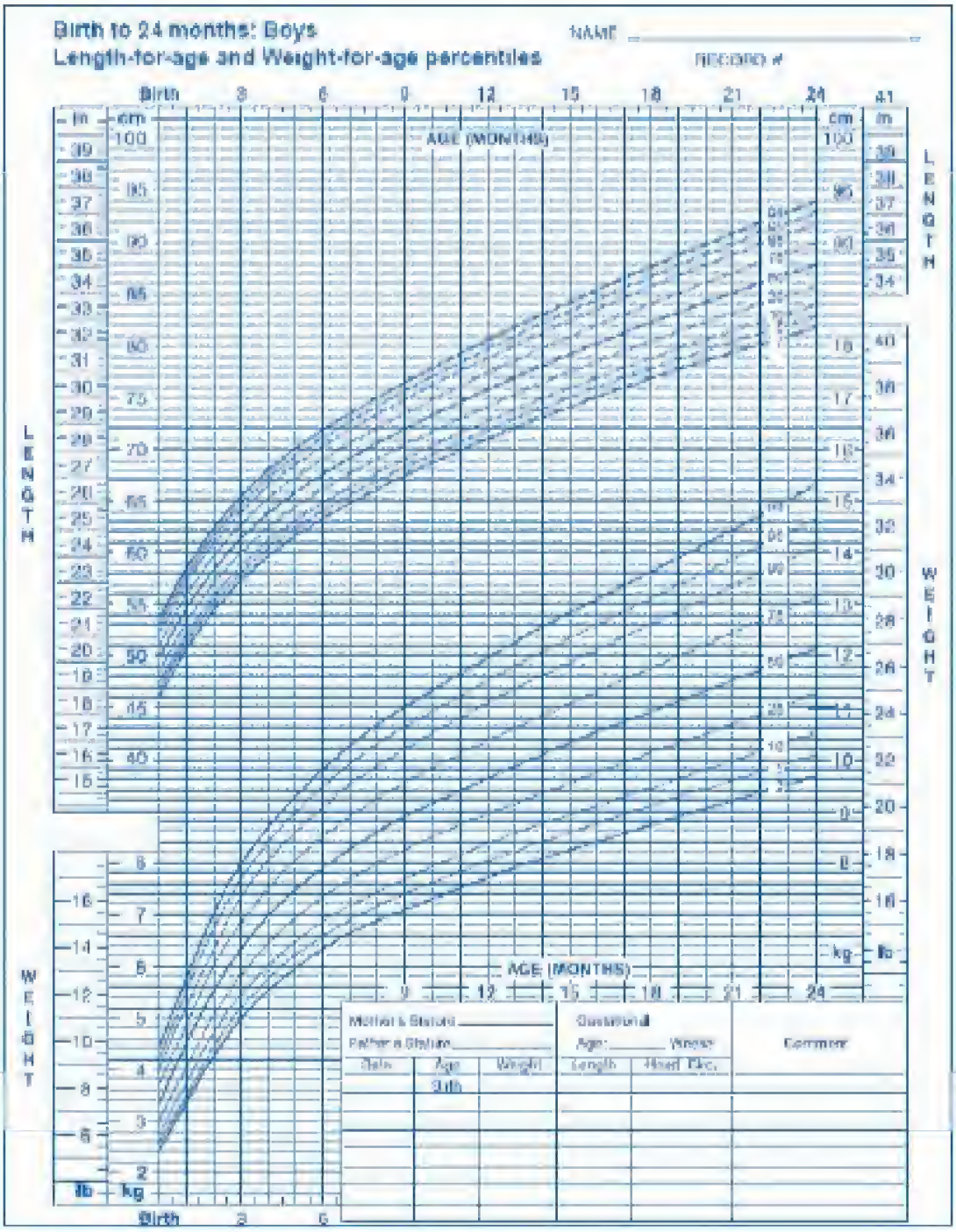
Rate of growth is maximal in infancy and during pubertal spurt

N.B

- Weight for height below the 5th percentile remains the single best growth chart indicator of acute under nutrition
- Decreased height for age with normal weight for age indicate nutritional disorder in the past
- Decreased both weight for height with normal height for age indicate both recent and past nutritional disorder
- Specialized charts have been developed for children with :
  - Very low birth weight and prematurity
  - Down
  - Turner
  - Klinefelter syndromes
  - Achondroplasia

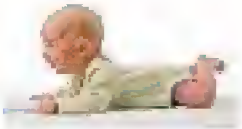
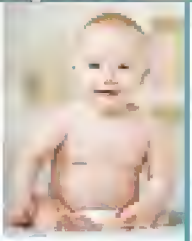
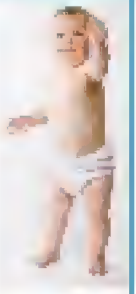
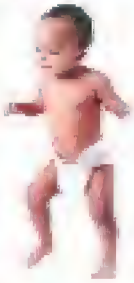
Examples of centile charts




Birth to 24 months: Boys
Length-for-age and Weight-for-age percentiles
NAME
RECORD #
AGE (MONTHS)
LENGTH
WEIGHT
Mother's Stature
Father's Stature
Date
Age
Weight
Length
Head Circ.
Comment

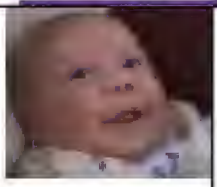
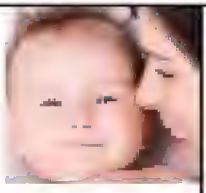
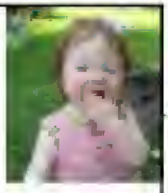
Assessment Of Development

Motor Milestones : (Locomotor development)

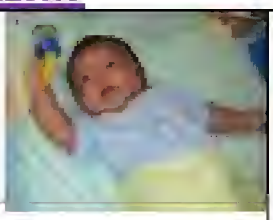
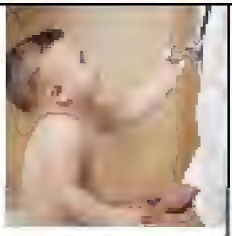
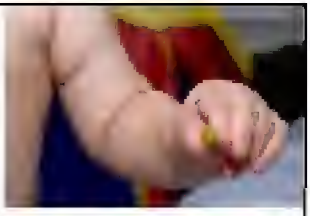
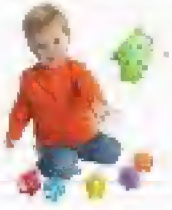
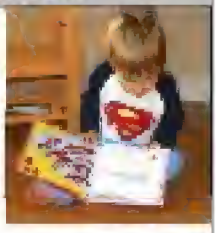
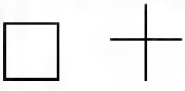
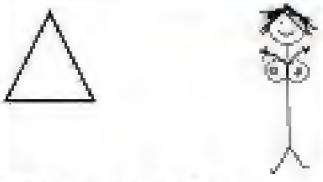
 Head support ; no head lag	 Sit without support	 Crawls
3 months	**6 months**	**9 months**
 Stands	 Walks	 Runs
10 months	**12 months**	**18 months**
 Climbs stairs	 Rides a tricycle	 Dresses himself
2 years	**3 years**	

Mental milestones

A. Social development

 Social smile on social contact	 • Recognizes mother • Excited at sight of food	 • Recognizes father • Stranger awareness	 • Finger feeds • Waves bye bye
2 months	**4 months**	**9 months**	**12 months**

B. Fine motor

4 months	6 months	9 months
		
• Play with hands in midline • Grasp offered rattle	• Outreaches objects, mouth it and transfers it	• Pincer grip
12 months	**15 months**	**18 months**
		
• Casting	• Tower of two cubes • Scribbles	• Turn pages in 2-3 pages
3 years	**4 years**	**5 years**
		
• Cut with scissors • Copies a circle	• Copies a cross & square • Recognize 3 colors	• Copies a triangle • Draws man with six parts

C. Speech development

At - 10 months → Says Mama or Dada
- 1 year → Speaks first real 3 words
- 19 months → Speaks 2-word sentences (e.g., "Mommy shoe")
- 2 years → Says 3 word sentences (phrases).
- 3 years → Says his name & age
- 5 years → Says clear speech

Criteria of speech delay

- No first words by 15 months.
- No real words by 18 months.
- No word combinations by 2 yrs
- Speech is difficult for others to understand at 3 years

D. School achievement

Self Assessment Clinical Cases

Case 1

A 3-month-old girl, comes in for her checkup with her mother .her mother complains that her baby is not active, sleeps much and cries little with persistence of the yellow tinge of skin and sclera since the first week of life. You requested a plain radiograph for her knees

a. **What does the x ray show?**
b. **What is the expected diagnosis?**
c. **What do you expect from examining her fontanels?**

Case 2

Bone age will be advanced in short stature caused by which of the following?

a. Environmental deprivation syndrome
b. Hypopituitarism
c. Hypothyroidism
d. Congenital adrenal hyperplasia
e. Chronic administration of glucocorticoids in high doses

Case 3

An infant can lift his head from a prone position 45° off the examining table, smiles when encouraged, and makes cooing sounds. He cannot maintain a seated position. The most likely age of the infant is

a. 1 month
b. 3 months
c. 6 months
d. 9 months
e. 12 months

Case 4

A child is brought to your clinic for a routine examine. She can dress with help, can ride a tricycle, knows her own age, and can speak in short sentences. She had difficulty in copying a square. The age of this child is most likely

a. 1 year
b. 2 years
c. 3 years
d. 4 years
e. 5 years

(Source: Pretest Pediatrics for USMLE)

Infant feeding

Breast Feeding

Control of milk production

1. Maternal Reflexes

1. Prolactin (Production) reflex

⇓

Suckling of nipple

↓

+ + vagus nerve

↓

+ + hypothalamus

↓

+ + anterior prtuitary

↓

↑↑ prolactin

↓

+ + milk secretion

2. Milk ejection (let down) reflex

⇓

Suckling of nipple

↓

+ + vagus nerve

↓

+ + hypothalamus

↓

+ + posterior pituitary

↓

↑↑ oxytocin

↓

+ + milk ejection.

2. Infant Reflexes

- Rooting reflex: Infant turns his head to the side where the nipple is felt
- Suckling reflex: Rhythmic movements of the mandible
- Swallowing reflex (Coordinated suckling and swallowing occurs in babies born after 34 completed weeks)

N.B: Maternal anxiety, stress and fatigue inhibits ejection reflex

Breast milk flow is maintained by

1. Mechanical factors: The main stimulus for breast milk flow .It is achieved by:
   - Suckling: the more regular & vigorous suckling, the more the milk flow.
   - Suckling initiate prolactin and milk ejection reflexes
2. Good maternal nutrition with plenty of:
   - Sugary fluids (not evidence based)
   - Vitamins B complex
3. Good maternal psychology (maternal anxiety & stress inhibits ejection reflex)
4. Hormonal balance
5. Rooming in (keeping the baby in mothers room) and skin to skin contact.
6. Demand feeding (feeding according to the infant desire)

Disadvantages of breast milk

1- Breast milk protein Allergy → very rare condition

2- Breast milk jaundice may occur due to pregnandiol secreted in breast milk.

3- Deficient Content of:

* Vitamin K; to avoid bleeding tendency, 1 mg Vit. K is given IM at birth
* Vitamin D and Iron:

American Academy of Pediatrics recommends supplementation with:

- Begin daily oral vitamin D drops (400 IU) at hospital discharge
- Iron (1-2 mg/kg/d) starting at age 4–6 months until age 1 year

4- Some Drugs are secreted in breast milk e.g. cytotoxics and antithyriod drugs

5- Some viruses are Excreted in breast milk e.g. CMV and HIV

Breast Milk Composition

✧ Colostrum → milk from birth to the 5th day of life

✧ Transient milk → milk from the 5th day to 21st day

✧ Mature milk → milk after the 21st day.

	Colostrum	Mature milk
Amount	40-60 ml	1 liter
Reaction	Slightly alkaline	Neutral
Color	Lemon yellow	Whitish
Consistency	Thick	Thin
Caloric value	57 cal/dl	67 cal/dl
Specific gravity	1040 – 1060	1030 – 1035
Protein	7 gm%	1.2 gm%
Fat	3 gm%	4 gm%
Carbohydrates	4 gm%	7 gm %
Colostrum corpuscles (Large endothelial cells from breast acini or fat laden leucocytes)	Normally present	Absent (if exist, it denotes deteriorating breast milk secretion)
Value	1. Nutritive (↑ protein) 2. Protective → ↑↑ Ig A & ↑ PMNLs & monocytes 3. Initiate gastrocolic reflex → mild laxative	See later

Advantages of Breast Feeding

The AAP and the WHO recommend that infants should be exclusively breastfed or given breast milk for 6 months. The decision to breastfeed should be considered a public health issue and not only a lifestyle choice

I. Advantages to the mother

1- Help involution of the birth Canal and reduce risk of post partum hemorrhage.
2- Natural method of Contraception.
3- Reduce the incidence of Cancer breast.

II. Advantages to the infant

A. Qualitative differences between human and cow's milk

	Human milk	Cow's milk
1.Protein		
a. Dietetic protein		
- Soluble (lactalbumin)	- 60%	- 20%
- Insoluble (casein)	- 40%	- 80%
- Soluble /Insoluble ratio	- 3:2 Protein is fine and thin and easily digested	- 1:4 Protein is tough & thick And hardly digested
b.Non dietetic protein		
- Lactoferrin level	- High → Static to E.coli → ↑ iron absorption → Immunomodulator	- Traces
- Immunoglobulins	- High (specific to human Pathogens)	- Traces (Specific to animal pathogens)
- Lysozymes level	- High → bactericidal	- Traces.
- Essential amino acids	- High → essential for brain development	- Traces.
2. Fat		
- Fat globules size	- Smaller size → easy digestion	- Larger size → hard digestion
- Diurnal variation	- Present → high concentration at the evening & end of feed	- Absent
- Lipase enzyme level	- High → help digestion	- Lower level
- Essential fatty acids	- Higher (11%) especially Leinoleic and oleic acids.	- Lower level
- Volatile fatty acids.	- Low level → less GIT upsets	- High → frequent GIT upsets→ regurgitation & distention

3. Carbohydrate	- β lactose → no fermentation (no gases nor vomiting) - Some is converted to lactic acid: → ↑ Calcium absorption. → Bacteriostatic effect	- α lactose → high incidence of fermentation → excess gases, and vomiting.
4. Minerals		
- Amount	- Low	- High → high risk of hypernatremia
- Calcium/Phosphate ratio	- 2/1 ; so absorption is better and rickets is less common	- 4/3 so less absorption → high risk of rickets
- Sodium content	- Low (less renal solute load)	- High
- Iron	- Low with good absorption sufficient for 1st 4 – 6 months	- Very low with bad absorption (less bioavailable)
5. Bacterial content	- Sterile	- Liable to contamination

Breast milk contains numerous growth factors e.g.

- Epidermal growth factor: promote repair of intestine
- Transforming growth factor (TGF): Promotes epithelial cell growth
- Nerve growth factor: Promotes neural growth

Breast milk is suggested to protect against: acute diarrhea, otitis media, urinary tract infections, necrotizing enterocolitis, DM, Crohn, Celiac and Cancer

Breast milk for premature is characterized by

1. Protein is higher by **20%** with higher immunoglobulins and lactoferrin.
2. Fat is higher by **50%** with higher content of long chain polyunsaturated fatty acids, which are essential for brain and retinal growth.
3. Vitamins → higher content of vitamins A & E.
4. Carbohydrate → lower lactose content.
5. Contain platelet activating factor acetyle hydrolase & IL-10 which protect against necrotizing entero colitis (NEC)

- Human milk has concentrations of calcium and phosphorus that are appropriate for full-term infants.
- These amounts are inadequate for the very low birth weight (VLBW) infant. Breast milk should be supplemented with additional calcium, phosphorus, and vitamin D, which can easily be done with a powdered human milk fortifier (Enfamil Human Milk Fortifier, Similac Human Milk Fortifier) (Nelson textbook of pediatrics)

B. Anti-infective properties of breast milk

I. Humoral immunity

1. **Breast milk contain Antibodies (humoral immunity) against**
   - Viruses: e.g. Poliomyelitis, mumps, rota virus.
   - Enteric bacteria: e.g. E.coli, cholera.
2. **Anti staph factor**: a polyunsaturated fatty acid.
3. **Anti-protozoal**: Lipase enzyme kills Entameoba histolytica & Giardia lamblia
4. **Antimicrobial enzymes**
   - Lyzozyme
   - Lactoperoxidases
5. **Bifidus factor**
   - Nature: Amino sugar
   - Role: stimulate growth of lactobacillus bifidus which is a normal bacteria flora in the intestine → interference with pathogenic bacteria as E. coli & vibrio cholera.
6. **Binding proteins**
   - Nature
     - Folic acid binding protein.
     - B_{12} binding protein.
     - Lactoferrin; Iron binding protein
   - Role: Folic acid, B_{12}, and iron are essential for growth of pathogenic bacteria ; binding proteins deprive pathogenic bacteria from these growth factors with subsequent bacteriostasis.

II. Cellular immunity

a. **Polymorphnuclear leucocytes and macrophages** which can
   - Secrete lysozymes, complement, and lactoferrin
   - Phagocytose and kill bacteria and fungi

b. **Lymphocytes**:
   - T lymphocytes provide cell mediated immunity
   - B lymphocytes secrete antibodies ; mainly IgA

III. Others

- Low buffering effect: neutral or slightly alkaline milk pH preserves gastric acidity which acts as a barrier against infection
- Low incidence of necrotizing enterocolitis (NEC)
- Oligosaccharides and κ-casein: Prevent bacterial attachment
- Nucleotides: Enhance antibody responses and bacterial flora

Efficiency (Adequacy) of breast feeding

Evidence of adequate feeding

1. Adequate weight gain on serial assessments (the most important clue)
2. Satisfaction after feeding; the baby sleeps 2-3 hours after feedings
3. Normal bowel habit: no diarrhea or constipation
4. Normal urine flow
5. Test feed
   - Weigh the infant before & after feeding with unchanged clothes 6 times a day
   - Calculate amount of the feed for 3 days and then take the average

Abnormalities of breast feeding

	Under feeding	Over feeding
Manifestations	* Exaggerated initial weight loss Followed by poor weight gain * None satisfaction post feed - Stay suckling for longer - Stay alert after feeds - Excessive crying - Sucking fingers (hungry!!) * Delayed stooling * Oliguria * Hypernatremic dehydration may occur	* Excessive weight gain * Excessive crying & irritability due to colic and distension * Repeated vomiting * Bulky stool (may be diarrhea) * May be polyuria * May be sore buttocks.
Management	* Direct observation of breast-feeding can help identify improper technique * Examine both infant and Mum for a treatable cause * Supplemental formula	- Space feeds apart - No suckling > 20 min / feed. - Remove excess breast milk by pump post feeding

Intervals between feeds (Ideally 3 hours intervals = gastric emptying time)

2 hourly feeding for	4 hourly feeding for
• First 2 weeks of life. • Weak sucker • Scanty milk flow.	• After the 4th month. • Overweight and strong suckers. • Liberal milk flow.

Contraindications of breast feeding

I. Maternal causes

Temporary	Permanent
1. Bilateral nipple fissuring. 2. Bilateral acute mastitis & abscess 3. Infectious diseases e.g typhoid 4. Mothers on temporary medicines that is known be secreted in milk and may harm the baby	1. Malignancy 2. Active maternal CMV Infection 3. Maternal use of certain radioactive isotopes, cancer chemotherapy agents, and a small number of other medications (*See The Lacimed Database online for further details*)

Active, untreated maternal tuberculosis

A. **Current recommendation** (American Academy of Pediatrics, 2014):

- Baby is separated from mother until completion of 2 wk of maternal therapy
- During this period milk is expressed for the baby to be fed via bottle

B. Other opinion: Mums can lactate with the following precautions:

- Mum receives anti T.B drugs and uses mask during feeding
- The baby receives prophylactic isoniazid 10 mg/kg/d *(Window prophylaxis)*
  - Continued until the mother has been shown to be sputum culture negative for ≥3 mo
  - At that time perform Manteaux skin test
    a. Positive test: INH is continued for a total duration of 9-12 mo
    b. Negative test: stop INH & vaccinate the infant with INH resistant BCG
- Separation is considered if the mother:
  - Suspected to have drug resistant TB
  - Acutely ill
  - Non adherent to treatment

Infant to HIV mothers

- In USA :breast feeding is contraindicated
- In other regions: risk of viral transmission if feeding allowed must be weighed against risk of developing malnutrition if breast feeding withhold

Infant to HBsAg positive mothers

Breast feeding is allowed so long as the baby has received both the HBV vaccine & Ig

I. Infant causes

1. **Milk protein allergy**: Extremely rare.
   - C/P - Colic ,vomiting, diarrhea
     - May be bloody stool or occult blood in stool.
   - Treatment - Hypo allergenic formula

2. **Lactose intolerance**
   - Due to - Lactase deficiency ; primary or secondary to gastroenteritis
   - C/P - Accumulated lactose in intestine leads to:
     - Fermentation → abdominal distension ,colic &vomiting
     - Osmotic diarrhea → reducing substance in stool.
     - Change to lactic acid → acidic motions → perianal soreness → stool pH < 5
   - Treatment - Lactose free formula

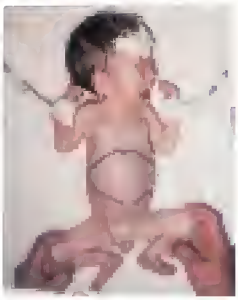
3. **Galactosemia**: Autosomal recessive disorder

   Normally: Lactose $\xrightarrow[\text{enzyme}]{\text{Lactase}}$ Glucose + Galactose -1-Phosphate (Gal-1-P)

   Gal-1-P $\xrightarrow[\text{Uridyle transferase}]{\text{Galactose 1 phosphate}}$ Glucose.

   In galactosemia : absent Gal-1-P uridyl transferase→ accumulated Gal-1-P leads to:
   - Cataract (absent red reflex in newborn)
   - Chronic active hepatitis, hepatomegaly
   - Mental retardation

   Treatment: lactose/galactose-free formula



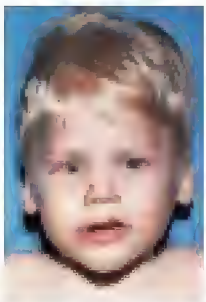
4. **Phenyleketonuria**: Autosomal recessive disorder

   Normally: Phenylalanine $\xrightarrow[\text{hydroxylase}]{\text{Phenylalanine}}$ Tyrosine & Tryptophan

   In phenylketonuria : Defective phenylalanine hydroxylase enzyme leads to:
   - Fair skin , hair and blue eyes
   - Cerebral palsy and seizures
   - Mental retardation.

   Diagnosis
   - Positive screening test of Guthrie
   - Phenylalanine > 1200 mol/L ÷ Normal / low tyrosine

   Treatment: Phenylalanine low formula (contain tyrosine)



Problems with breast feeding

Nipple Pain

- Common complaint in the immediate postpartum period
- Due to poor infant positioning and improper latch and or nipple candidiasis

Treatment

- Treat both mother and baby if candidiasis is found.
- If accompanied by engorgement, express milk manually until healing has occurred *(Breast milk can be refrigerated and used within 48 hours. Frozen milk can be used for up to 6 months-thawing should be by warm water but never in microwave!)*

Engorgement

- Incomplete removal of milk due to poor breast-feeding technique or other reasons such as infant illness
- The breasts are firm, overfilled, and painful

Treatment

- Frequent breast-feeding
- Manual milk expression before breast-feeding may be required.

Mastitis

- Presentation
  - After the 2nd post-delivery week
  - Usually unilateral localized warmth, tenderness, edema, and erythema.
  - Sudden onset of breast pain, myalgia, and fever.
- Organisms implicated
  Staphylococcus aureus, Escherichia coli, group A streptococcus, Haemophilus influenzae, Klebsiella pneumoniae, and Bacteroides spp.

Treatment

- Oral antibiotics and analgesics
- Promote breast-feeding or emptying of the affected breast
- Breast abscess: Intravenous antibiotics as well as incision and drainage, along with temporary cessation of feeding from that breast.

Jaundice

a. **Breast-feeding jaundice**

- Largely related to insufficient fluid intake
- Commonly associated with exaggerated physiologic weight loss ≥ 12%
- It may also be associated with dehydration and hypernatremia

b. **Breast milk jaundice** (See neonatology)

Artificial Feeding

Defined as supplying any milk other than breast milk

Indications

1. Substitutive feeding (all breast feeds are replaced by bottle feeds)
   - Absent mother
   - Contraindications to breast feeding (maternal or infant causes) .
2. Mixed feeding
   a. Complementary feeding (Breast feeds are completed by bottle feeds)
      - Indicated when breast milk is not enough (scanty breast milk secretion)
      - Precautions:
        - Breast milk should be given first and completely emptied.
        - The used milk should be humanized formulas.
        - Formula should not be sweetened
        - Bottles holes should not be large
   b. Supplementary feeding (some breast feeds are replaced by bottle feeds) for:.
      - Working mother.
      - Twin delivery (breast and bottle given to each baby alternatively)

Disadvantages: - Liable to Contamination.
- Costly
- Lack advantages of breast milk

1. Fresh fluid animal milks

Types:
* Cow's milk → most commonly used worldwide.
* Buffalo's milk → most commonly in Egypt.
* Goat's milk
* Ass milk → near in composition to human milk.

Specific disadvantages

A. Drawbacks of Goat's milk:
- Low folic acid →↑ incidence of megalobalstic anaemia
- High risk of brucellosis.

B. Drawbacks of cow milks:- (*See comparison between breast & cow milk*)
1. High incidence of diarrhea, respiratory infections & allergies
2. High risk of iron deficiency anemia due to:
   - Low iron content with poor absorption
   - Low lactoferrin content.
   - Occult blood loss due to heat labile protein.

2. Dried powdered milk formula

* Dried powdered milk formula are based on cow milk in most cases

Advantages

1- Can be modified, so Fits for different infant needs.

2- Fortified with vitamins , minerals, and trace elements

1. Humanized formulas

Modifications: Modified to be very similar to breast milk :

- Protein is modified to form a fine curd
- Carbohydrate content is increased.
- Fat is refined with increased poly unsaturated fatty acids
- Vitamins (especially vitamin D & C) are added
- Calcium: phosphate content reduced and ratio adjusted
- Trace minerals are added particularly Iron , copper & zinc

Indications : - Healthy infants when breast milk is scanty or unavailable

- Large prematures (2-2.5 kg)
- Milder degrees of malnutrition

Examples : - Novalac , Bebelac, Nan, Bionil, Aptamil

⇒ 1 spoonful (4gm) for each 30 ml water.

- Similac , S-26

⇒ 1spoonful (8gm) for each 60 ml water.

N.B (May be numbered as 1 for the 1st 6 months of life, 2 for the next 6 months of life, and may be 3 for after 1 year of life)

2. Lactose free formula

Modification : - Lactose is replaced by other sugar (sucrose or glucose)

Indications : - Lactose intolerance.
- Galactosemia

Examples : - Enfamil LactoFree, S26-LF, Isomil

3. Hypoallergenic formula

A. Casein hydrolysate based formula

1. Partially hydrolyzed

   Containing oligopeptides with a molecular weight of <5000 d

   Or

2. Extensively hydrolyzed

   Containing peptides with a molecular weight <3000 d.

Indications

- Prevent or delay atopic dermatitis
- Infants intolerant to cow's milk or soy proteins
- These formulas are lactose free and can include medium-chain triglycerides, making them useful in infants with malabsorption

Examples

- Aptamil Pepti 1 and 2
- Pepti junior
- Pregestimil

B. Amino Acid Formulas

Amino acid formulas are peptide-free formulas that contain mixtures of essential and nonessential amino acids.

Indications

- Infants with dairy protein allergy who failed to thrive on extensively hydrolyzed protein formulas
- For severe Cows' milk allergy, and multiple food protein intolerance

Examples

- Neocate LCP
- Nutramigen AA (Gluten & Lactose-free)
- EleCare (Similac)

N.B *(Soy protein based formula e.g. Isomil is not fit for cow milk allergy due to cross allergy but can be used as a lactose free formula)*

4. Preterm infant formula

Modification : - More protein , medium chain triglycerides, vitamins and calories(80 calories /100 ml)
- Lower lactose.

Examples : - Enfamil EnfaCare, Enfalac premature, Similac expert care

5. Pre-thickened formula

Indications : - Regurgitations and Gastro esophageal reflux disease

Modification - Contain pregelatinised rice starch or cooked corn starch

Precaution : - Not to be used for a period of > 6 months
- Not to be used in conjunction with antacid products

Example : - Enfamil AR

6. Amino Acid-Modified (Metabolic) Formulas

a. Phenylalanine low formula

Indications : - Phenyleketonuria

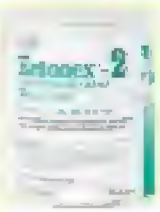
Example : - Lofenalac

b. Branched chain amino acid free formula

Nutrition support of children with maple syrup urine disease

Supplemented with L-carnitine and taurine

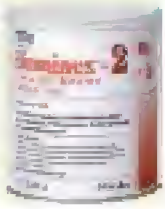
Example: Ketonex



c. Methionine-free formula

Nutritioa support of children with homocystinuria

Example: Hominex



7. Formulas for specific diseases

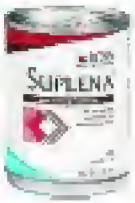
a. Nutrition support for babies with renal failure

Modifications:

- High calorie with low fluid volume
- Low salt , low protein
- Low potassium ,and phosphorus

Examples:

- Renastart
- Suplena
- Nepro



b. Nutrition support for children with acute or chronic liver failure

- Generaid
- Heparon Junior

Program of Artificial Feeding

1. **Decide type of milk**
   * According to:
     1. Whether the baby is healthy (R/ humanized formula) or not
     2. Financial conditions of the family
   * Use either:
     - Dried powdered milk
     - Fresh fluid animal milk(not preferred in the 1st year of life).

2. **Determine the amount of milk needed by**
   a- Age method
   - Valid only for healthy full term .
   - Amount of milk (ml/feed) = Age in days × 10
     Age in weeks × 10 + 70
     Age in months × 10 + 100

   b- Caloric(weight) method
   - this method is valid for both the healthy and diseased babies
   - More accurate than age method
   - Calculation:
     - Normal healthy infant needs 110 cal/kg/d.
     - Milk contain 67 cal/per 100 ml.
     - So total daily need of milk = 100/67 × (110 × body weight in kg).
     - This total amount is divided into feeds.

3. **Formula (concentration of milk)**
   i- Formula of dried powdered milks:
   - One measure of 4 gm diluted by 30 mL boiled water e.g. Bebelac
   - One measure of 8 gm diluted by 60 mL boiled water e.g. Similac

   ii- Formula of fresh fluid animal milk (not recommended !!!)

4. **Number of feeds per day**: According to age; roughly
   Between 0-4 months → every 3 hours
   Between 5- 8 months → every 4 hours
   Between 9-12 months → every 5 hours

5. **Determine method of feeding**: According to age & condition: Bottle, tube, or dropper

Weaning

Introduction of semisolid and solid foods besides breast milk or formula

Values

- Compensate for increasing infant needs that can not be fulfilled by breast milk alone.
- Train the gastrointestinal tract and train the baby to use cup and spoon.
- Supply vitamins and minerals e.g. A , D , C , iron , zinc and calcium

When to initiate?

* Begin weaning at 6 months of age: Why?
  - Maturation of digestive enzymes occur
  - Decline of minerals and vitamin stores
  - Caloric value of breast milk becomes inadequate.
* Never try before 4 months due to:
  - Digestive enzymes of the infant have not developed yet
  - Breast milk is sufficient in the 1st 4 months of life
  - Risk of developing allergies

When to complete?

* At 1.5 to 2 years

Guidelines of weaning? (By American Academy of Pediatrics; Nelson 2016)

- Serve foods immediate after preparation
- Stepwise weaning
  - Introduce 1 food at a time
  - Small amount of one food is started and increased gradually
  - Do not introduce other new foods for 3-5 days to observe for tolerance
  - Feed slowly, do not force; many trials may be needed as spitting can occur.
- During illness give breast feeding and increase food intake after the illness.
- At the proper age, encourage a cup rather than a bottle
- Energy density should exceed that of breast milk
- Iron-containing foods (meat, iron-supplemented cereals) are required
- Zinc intake should be encouraged with foods such as meat, dairy products, wheat, and rice
- Phytate intake should be low to enhance mineral absorption
- Breast milk: exclusive in the first 6 months and should continue to 12 mo
- Fluids other than breast milk, formula, and water should be discouraged

How to start? Suggested plan

Age	Suggested food
6 mo.	Cereals, cornflower puddings (Cerelac) ,biscuits
7 mo.	Rice , Rice pudding , cheese and mashed fruits
8 mo.	Vegetable soups in water and yogurt, egg yolk
9 mo.	Beans and vegetable soup in meat
10 mo.	Mashed liver and meat
11 mo.	Poultry and rabbits
12 mo.	Mashed red meat , fish
In the 2nd year	Other family foods including fresh animal milks

What food to avoid?

- Canned foods
- Salt and spices
- Use of whole Cow milk below 1 year
- Sugar : no sugar sweetened beverages
- Chocking foods(e.g. nuts, grapes, raw carrots) in the first 3-4 years
- Allergenic foods e.g. Egg white
- Fruit juices during the first 6 mo of life and limited amounts of juices thereafter (120-180 ml /day for ages 1-6 yr)

Problems with weaning

1- Allergies → may follow some new foods e.g eggs, ...
2- PCM → sudden weaning on starchy foods → Kwashiorkor (KWO).
3- Colic is common especially with:
   - Excess sugary fluids
   - Early aggressive weaning
4- Diarrheal disorders → gastroenteritis due to contaminated foods.
5- Dental caries: associated with excess carbohydrates and bottle feeding.
6- Delayed weaning may predispose to:
   - Marasmus
   - Iron deficiency anemia.
   - Rickets.
7- Some Diseases may manifest during period of weaning: e.g.
   - Favism
   - Celiac disease

Self Assessment Clinical Cases

Case 1

You are reviewing this 8 months old, breast fed baby boy who had gastroenteritis for the previous 2 weeks, now he is irritable, has distended abdomen, still having mild watery diarrhea and some peri anal soreness

a. **What is your diagnosis?**
b. **How can you confirm it?**
c. **What is your decision?**

Case 2

Lactating mother with an acute medical condition cannot feed her full term normal male infant 2 mo age & 4 kg weight for about 3 days. His grandmother will take care of him.

a. **What is the type of artificial milk appropriate for him?**
b. **What is the number of feeds/ 24 hr?**
c. **How much is the amount of milk required /feed?**
d. **How can she prepare the formula (concentration of milk given)?**

Case 3

A 10 months old, breast fed boy who was switched to cow milk at 9 months as his mother has to return work, the mother complains that her baby becomes irritable, with more frequent vigorous crying episodes , vomiting and distension with occasional bloody stool; his weight declined from 8.7 kg to 6.5 kg

a. **What is the provisional diagnosis?**
b. **What is the laboratory test required?**
c. **What is the preferred formula for this boy?**

Case 4

A list of artificial milks

A. Humanized formula
B. Lactose free milk
C. Premature formula
D. Phenylalanin low formula
E. Predigested formula
F. Hydrolyzed formula

From list above select the milk suitable for the following cases:

1. Diarrhea that continues for 2 weeks following an attack of Rota virus gastro enteritis
2. Diarrhea that continues for more than 2 months with failure to thrive
3. A 1.8 kg newborn that developed neonatal seizures who has fair skin and hair and whose urine shows abnormal urine aminogram
4. A 1.8 kg newborn who developed neonatal seizures and abnormal liver function and abnormal red reflex
5. A 1.8 newborn that just recovered from RDs

Nutritional disorders

Protein Calorie Malnutrition (PCM)

[Protein Energy Malnutrition ;PEM]

Classifications of PCM

1. **Wellcome classification**: Based on weight for age & presence of edema.

Ratio of current weight to expected weight for age	Symmetrical Oedema	Diagnosis
> 80%	+ +	Nutritional edema or KWO
60-80%	- -	Simple underweight
60-80%	+ +	Kwashiorkor (KWO)
< 60%	- -	Marasmus
< 60%	+ +	Marasmic KWO

2. **Waterlow Criteria**

A. Changes in weight may be an indicator of acute malnutrition.

$$\frac{\text{Actual wt (kg)} \times 100}{\text{Expected wt for ht at } 50^{th} \text{ centile}}$$

- Grade 0 : ≥90% → Normal
- Grade I : 80%–89% → Mild
- Grade II : 70%–79% → Moderate
- Grade III : <70% → Severe

B. Changes in height may be an indicator of chronic malnutrition.

$$\frac{\text{Actual ht (cm)} \times 100}{\text{Expected ht for age at } 50^{th} \text{ centile}}$$

- Grade 0 : ≥95% → Normal
- Grade I : 90%–94% → Mild
- Grade II : 85%–89% → Moderate
- Grade III : <85% → Severe

3. **WHO criteria**
   - Wasting: Low weight for height(WFH) below the median
   - Stunting : Low height for age (HFA) below the median
4. **Kanawati criteria**
   - Uses MUAC divided by occipitofrontal head circumference(see before)
   - Malnutrition degree: Mild < 0.31 , moderate <0.28 , severe <0.25

(Nelson Textbook of Pediatrics and Texas Children's Hospital Handbook of Pediatrics, 2016)

Kwashiorkor (KWO)

(Edematous PCM, Red Baby)

Definition

- Acute protein deficiency with normal or even high caloric intake
- "The sickness the baby gets when the new baby comes" in Ghana language

Incidence

- More frequent in babies whose mums are poor , and ignorant
- KWO usually affects infant ages between 6 months to 2 years

Causes

Main factor

- Sudden faulty weaning on starchy, carbohydrate, protein deficient diet.
- Maternal deprivation: the 1st baby is neglected (affected) when a 2nd is born

Contributing factors :infections e.g.

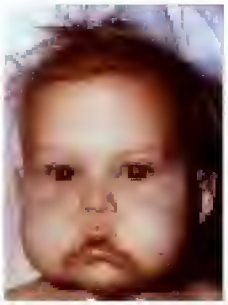
- Pertussis → recurrent vomiting.
- Chronic diarrhea and parasitism → protein loss in stool.
- Measles → complicating enterocolitis.

Clinical Picture

Constant features

1. Edema

- Starts in the dorsa of feet & hands then the upper and lower limbs
- Edema is bilateral, pitting & painless



- Facial edema produce prominent pale cheeks → Doll facies
- Periorbital edema

- With shiny overlying skin
- Ascites and pleural effusion are usually absent

Etiology of edema

- Hypoalbuminemia → reduced plasma osmotic pressure
- Decreased anti-oxidants →*free radical* damage → ↑ capillary permeability
- Other proposed causes: ↓ Na/K-ATPase activity & aflatoxin poisoning
- Increased Aldosterone and ADH→ salt and water retention

Grading of edema

- Grade 1: mild edema on both feet or ankles
- Grade 2: moderate edema on both feet, lower legs, hands, or lower arms
- Grade 3: severe generalized edema affecting limbs & face

2. Mentality changes

- Patient looks dull , apathetic, miserable, disinterested in surroundings with marked anorexia
- Global developmental delay in severe malnutrition

Due to

* ↓ Aromatic amino acids → ↓ Neurotransmitters
* Maternal deprivation.

3. Growth retardation

- Failure to gain weight followed by weight loss
- Length is much less affected as KWO is acute disease.
- Weight loss may be masked by edema and preserved subcutaneous fat

4. Muscle wasting

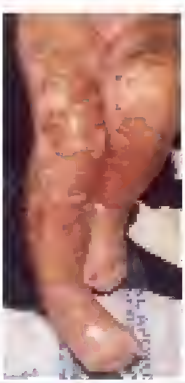
- Muscles are thin, atrophic & weak
- Decreased mid upper arm circumference < 12 cm
- Head circumference / chest circumference ratio > 1

Variable features

1. Hair changes

- Hair is lusterless , brittle, sparse, easily pickable
- Progressive lightening of hair; black → brown → reddish → yellow→ gray
- Flag sign:
  - Alternating bands of light color & normal color
  - In long haired with relapses of malnutrition
- Due to tyrosine and copper deficiency (essential for melanin synthesis)

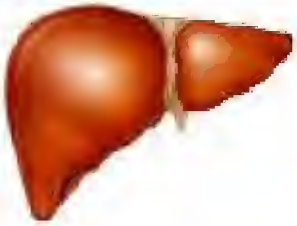
2. Skin changes



- Starts as dry scaling skin → erythema → hyperpigmentation & desquamation (Crazy paving or Flaky paint dermatosis)
- Skin infection is common
- Possible causes:
  - Vitamin A deficiency
  - Essential fatty acids deficiency
  - Zinc deficiency

3. Hepatomegaly

- Caused by fatty infiltration due to decreased lipotropic factors
- No hepatocyte damage (No cirrhosis)
- Hepatomegaly is reversible with treatment.
- Size may increase at the start of treatment if high caloric diet is used due to accumulation of glycogen before disposing fat (nutritional recovery syndrome)



4. GIT manifestations

- Diarrhea due to gastroenteritis and /or Malabsorption
- Abdominal distension may be due to malabsorption or hypokalemia

5. Anemia: May be due to:

- Iron deficiency → hypochromic microcytic anemia
- Protein deficiency → normochromic normocytic anemia
- Folic acid and/or B_{12} deficiency → megaloblastic anemia

6. Vitamin deficiency

- Vitamin A deficiency (very common) manifested by:
  - Eyes : - Xerosis, Bitot spots
    - Keratomalacia
    - Corneal ulcers and eventual scarring
  - Mouth : stomatitis.

- Vitamin C → spongy bleeding gums
- Vitamin B_2 deficiency : cheilosis, angular stomatitis.
- Vitamin D deficiency : it is usually not manifest due to arrested growth
- Vitamin K deficiency → bleeding tendency.

Complications(DIE B H4)

1- Dehydration: Due to gastro enteritis & anorexia.

2- Intercurrent infections:e.g.

- Gastro enteritis
- TB & bronchopneumona
- Oral moniliasis
- Noma : It is chronic necrotizing ulceration of the gingiva and the cheek
  - May be incited by *fusobacterium necrophorum & prevotella* co infection
  - Manifestations: fever, malodorous breath, anemia, leukocytosis

3- Electrolyte disturbances:

- Hyponatremia
- Hypokalemia
- Hypocalcemia & hypomagnesemia ⇒ may be tetany

4- Blindness: due to keratomalacia secondary to severe vitamin A deficiency

5- Hypothermia
6- Hypoglycemia: Commonly associated with sepsis
7- Heart failure due to:
- Severe anemia.
- Volume overload.
- Weak myocardium ⇒ dilated cardiomyopathy.

8- Hemorrhage due to:
- Vitamin K deficiency.
- Disseminated intravascular coagulation (DIC)

Investigations

1. To support the diagnosis
- Plasma proteins:
  - Decreased total plasma proteins < 4.5 gm /dl(normal 6-8 gm/dl).
  - Decreased albumin < 2.5 gm / dl (normal 3.5 – 5 gm/dl).
- Non essential / essential amino acids > 3 (normally ≤ 2 ,between 2-3 in subclinical cases)

2. To detect complications
- Monitor blood glucose closely
- CBC for anemia and leukocytosis in infection
- Sepsis workup e.g. CBC with differential, CRP, urinalysis, stool analysis, blood culture, chest x ray and tests for tuberculosis
- Serum electrolytes/minerals: Na, K, Ca, Mg.

Incomplete KWO (Pre KWO)

The patient shows all constant features of KWO except oedema & all variable features except skin changes

Phenomena which may occur during KWO treatment

1. **Hypokalemia:** Hypokalemia (already present) is aggravated by glucose infusion
2. **Circulatory overload:**
With infusion of large doses of blood or plasma →↑ plasma osmotic pressure → shift of fluid from interstitial compartment to intravascular compartment → volume overload & heart failure.
3. **Initial weight loss:** May occur due to absorption of edema fluid.
4. **Nutritional recovery syndrome** may rarely occur due to either:
A. Excess caloric intake → excess glycogen deposition in the liver before disposing excess fat → hepatomegaly may increase at the start of treatment
B. Excess protein intake > 6 gm/kg/d → liver is exhausted by protein metabolism
⇒ Excess ammonia load on the liver leads to:
1. Hepatic encephalopathy with lethargy, convulsions & coma.
2. Hepatocyte necrosis → liver cell failure with hepatomegaly, jaundice, ascites and even liver cirrhosis later on.

Marasmus

(Failure to thrive or non oedmatous PCM with severe wasting)

Definition: Chronic under nutrition with deficiency of both proteins & calories.

Causes

I. Primary (Dietetic)

- Target age: 6 months – 2 years
- Usually in low socioeconomic classes where the mothers are ignorant
- Inadequate food intake due to

A. Low quantity
- Scanty breast milk in breast fed infants
- Scanty or infrequent feeds in artificially fed
- Low caloric diet in older infant

B. Poor quality
- Prolonged breast feeding without supplementation
- Diluted formula in artificially fed
- Reliance on fluids

C. Feeding difficulties: e.g. with bilateral cleft lip and /or palate

II. Secondary (Non dietetic)

1. **Preterms and twins**: are more prone to maramsus due to:
   - High rate of growth in face of weak suckling power and limited capacity for digestion and absorption
   - Limited fat stores
2. **Chronic infections**
   - Examples: Tuberculosis, empyema, chronic pyelonephritis, etc…
   - Mechanism : Anorexia & hypercatabolic state
3. **Malabsorption states/Metabolic diseases**
   - Recurrent gastro enteritis / Chronic diarrhea
   - Malabsorption syndrome due to e.g., Cystic fibrosis, celiac disease.
   - Inborn errors of metabolism e.g. Galactosemia ,organic acidemias
4. **Pediatric malignancies**: via anorexia, hypercatabolism & chemotherapy
5. **Congenital anomalies**
   - Neurologic: e.g. cerebral palsy, mental retardation.
   - Congenital heart diseases
   - Gastrointestinal e.g.
     - Gastroeosphageal reflux disease.
     - Congenital pyloric stenosis.
   - Renal anomalies (due to associated UTI & acidosis).
6. **Maternal neglect** (child abuse; non organic failure to thrive)

Pathophysiology of Marasmus

- In infants the daily caloric intake is consumed as follows:
  - Basal metabolic rate (BMR) 50 % ⇒ unavoidable
  - Physical activity 25 %
  - Growth 12 %
  - Losses and others 13 % ⇒ unavoidable.
- When there is caloric deficiency the first compensatory mechanism will be decrease physical activity and arrested growth. With advanced caloric deficiency the body utilizes his own tissues; firstly fat then proteins to maintain BMR which results in marasmus.

Clinical picture

I. Symptoms: (5C)

- Failure to gain weight followed by progressive weight loss(Cachexia)
- Baby is usually hungry: irritable, Crying, sucking fingers with little sleep.
- Constipation due to reduced food intake but may be diarrhea due to starvation (greenish, scanty, offensive with mucus & debris) , gastroenteritis ,malabsorption or maldigestion
- May be features suggesting the Cause
- May be features of Complications e.g. gastro enteritis, pneumonia.

II. Signs

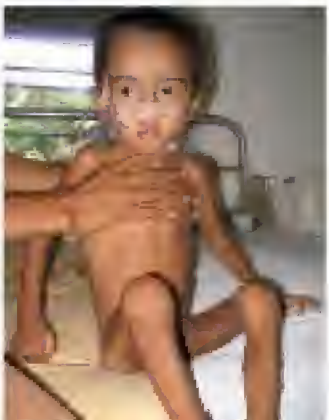
A. Protein deficiency manifestation

1. Body weight is less 60% of the normal weight for age without oedema.

- Loss of 40% of pre illness body weight → 1st degree marasmus
- Loss of 40-50% of pre illness body weight → 2nd degree marasmus
- Loss of > 50% of pre illness body weight → 3rd degree marasmus

2. Muscle wasting

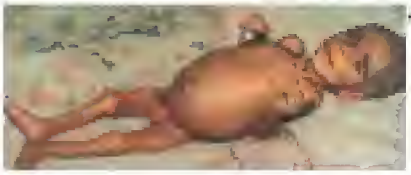
- Muscle is sacrificed to keep near normal plasma proteins.
- Muscle wasting is more severe in marasmus than in KWO giving rise to stick like appearance of limbs
- Muscle wasting is detected by decreased MUAC and chest circumference.



B. Caloric deficiency manifestation

1. Loss of subcutaneous fat from

- Abdominal wall (1st degree marasmus)
- Buttocks & limbs (2nd degree marasmus)



- Cheeks (senile face) (3rd degree marasmus)

The buccal pad of fat is the last to be lost as it is unsaturated fat essential for suckling

Outcome

- Skin becomes thin, loose, wrinkled, thrown into folds especially on the medial aspect of the thighs.
- Decreased triceps skin fold thickness
- Prominent normal costochondral junctions in marasmus due to loss of subcutaneous fat are called false rosaries.

2. Hypothermia due to

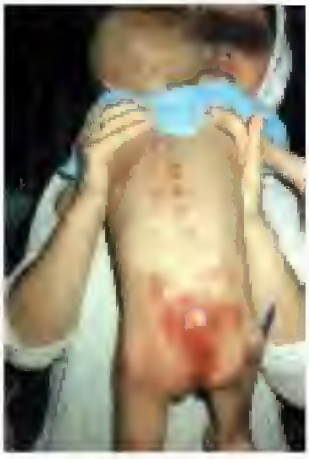
- Loss of subcutaneous fat → excess heat loss.
- Hypoglycemia → decreased basal metabolic rate.
- Septic shock.

C. Vitamin deficiency, anemia, hair & skin changes may occur as in KWO

D. Signs of an underlying cause in secondary marasmus

Complications

As in kwashiorkor plus (MOAP)



1- Muscle fibrosis in advanced cases

2- Oedema may occur with development of marasmic kwashiorkor

3- Atrophic ulcers over bony prominences

4- Purpura due to DIC due to dehydration, toxemia, acidosis

Investigations

1. Biochemical changes in marasmus

Blood : - Hypoglycemia (due to reduced glycogen stores in the liver).
- Plasma proteins slightly reduced

Urine: - Ketonuria (fat hypercatabolism).
- Increased creatinine (muscles hypercatabolism)

2. For a cause in the secondary marasmus

1- Stool analysis for parasites, stool cultures and *malabsorption workup*

2- Urine analysis and culture

3- Abdominal sonography.

4- Organ function tests (renal & liver functions tests)

5- Others :e.g.

- Chest x-ray
- Tuberculin test: is commonly negative due to 2^{ry} immunodeficiency
- Echocardiography for suspected congenital heart diseases.
- Barium study , endoscopy ± biopsy for suspected GIT diseases

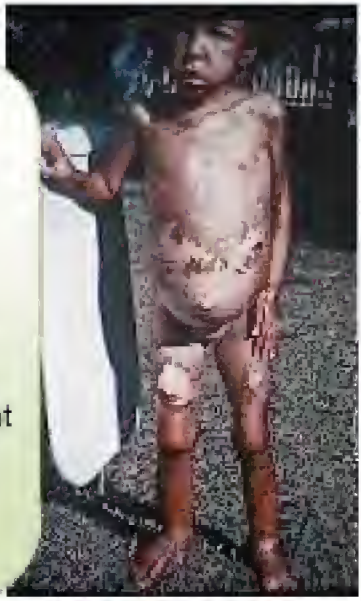
3. For complications ⇒ as in KWO

Death May occurs in severe complications especially due to:

- Hypoglycemia
- Shock (septicemia or dehydration) → disseminated intravascular coagulopathy
- Heart failure

Marasmic KWO: is manifested by:

- Weight < 60% of expected for age with nutritional oedema(*wasting &edema*)
- MUAC< 11 cm with edema
- It occurs mainly in marasmic child fed on carbohydrate diet only without adequate protein → appearance of oedema → marasmic KWO
- Other features of marasmus : loss of subcutaneous fat and marked muscle wasting are present
- Other features of kwashiorkor: mentality changes , dermatosis and hair changes are present



Failure to thrive: this term is considered if

- Child's weight is below the 5th percentile, or
- Child's weight drops down more than 2 major percentile lines in short time, or
- Child's weight for height is less than the 5th percentile.
- Etiology & management: Same as marasmus.

2. For a cause in the secondary marasmus

1- Stool analysis for parasites, stool cultures and *malabsorption workup*
2- Urine analysis and culture
3- Abdominal sonography.
4- Organ function tests (renal & liver functions tests)
5- Others :e.g.
- Chest x-ray
- Tuberculin test: is commonly negative due to 2^{ry} immunodeficiency
- Echocardiography for suspected congenital heart diseases.
- Barium study , endoscopy ± biopsy for suspected GIT diseases

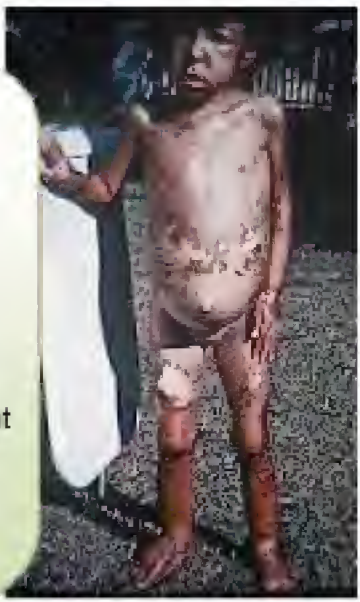
3. For complications ⇒ as in KWO

Death May occurs in severe complications especially due to:

- Hypoglycemia
- Shock (septicemia or dehydration) → disseminated intravascular coagulopathy
- Heart failure

Marasmic KWO: is manifested by:

- Weight < 60% of expected for age with nutritional oedema(*wasting &edema*)
- MUAC< 11 cm with edema
- It occurs mainly in marasmic child fed on carbohydrate diet only without adequate protein → appearance of oedema → marasmic KWO
- Other features of marasmus : loss of subcutaneous fat and marked muscle wasting are present
- Other features of kwashiorkor: mentality changes , dermatosis and hair changes are present



Failure to thrive: this term is considered if

- Child's weight is below the 5th percentile, or
- Child's weight drops down more than 2 major percentile lines in short time, or
- Child's weight for height is less than the 5th percentile.

♦ Etiology & management: Same as marasmus.

Management of PCM

A. Prevention

- Providing micronutrient interventions such as vitamin A and iron supplements for pregnant and lactating women and young children
- Encourage exclusive breast feeding
- Proper weaning .
- Regular check of growth by growth curves to pick early malnutrition which appear as flatting of weight curve
- Deworming in endemic areas & oral rehydration in high-diarrhea regions
- Fortifying commonly eaten foods with micronutrients (such as salt fortified with iodine) and foods like wheat, oil, and sugar with iron, vitamin A, and zinc

B. Curative

I. Inpatient or outpatient care?

- Outpatient care for clinically well, uncomplicated and with good appetite
- Inpatient care for complicated cases, cases with severe edema and marasmus kwashiorkor pateints

II. Stabilization phase (In the 1st 1- 7 days) for:

Hypoglycemia

- Glucose 10% oral, or intra venous
- Frequent feeding ; 2 hourly day & night.

Hypothermia

- Proper wrapping/ Warmers
- Treat hypoglycemia & serious systemic infections

Dehydration:

- Preferably oral rehydration solution (ReSoMal)
- Continue breast feeding
- Intra venous fluids for severe dehydration.

Hypoglycemia, hypothermia and dehydration have priority for treatment in the first 1-2 days of management

Electrolytes and minerals correction

- Monitor and correct levels of phosphate, potassium, calcium and magnesium especially with start of feeding (see refeeding syndrome)

Infections

- Appropriate antibiotics
- Specific e.g. Anti tuberculous for T.B.

Heart failure

- Packed RBCs for anemic heart failure
- Diuretics, vasodilators and cautious use of digitalis

Blood transfusion

- Fresh whole blood transfusion for severe anemia: 20 ml/kg for marasmus and 10 ml/kg for KWO.
- Fresh packed RBCs for severe anemia with anemic heart failure: 10 ml/kg for marasmus and 5 ml/kg for KWO

III. Dietetic treatment

Route

- Preferably oral
- Nasogastric tube for cases with severe anorexia

Amount

- Start at 80-100 cal./kg/day in stabilization phase
- Increase gradually in *Rehabilitation phase* (2^{nd} - 6^{th} week) to a target of 150-220 kcal/kg/d
- Fluid 130 ml/kg/d (100 ml/kg/d if the child has severe edema) of low osmolality and low lactose feeds
- Small frequent feeds every 2-3 hours day and night increased gradually over 1-2 weeks in strength & amount as the appetite improves

Protein intake

- Start with 1-1.5 gm/kg/d and increase gradually to 4- 6 gm/kg/d

Type of food

- If the child is breastfed, encourage to continue breastfeeding but give the prescribed amounts of starter formula (F-75) to make sure the child's needs are met
- Severe malnutrition between 6 – 60 months of age benefit from

Powdered milk–based foods (Formula diets)

- F75 (75 cal/100ml without iron) for initial feeding.
- F100 (100 cal/100ml with iron) is used later in the rehabilitation phase

Ready to use therapeutic foods (RUTF)

- A mixture of powdered milk, peanuts, sugar, vitamins, and minerals
- Much better than formula diets

III. Supportive treatment

1. Multivitamins especially
   - Thiamin / Vitamin B complex, Vitamin A
   - Vitamin D: prevents rickets during period of catch up growth.

2. Minerals especially
   - Phosphorus
   - Magnesium
   - Calcium
   - Zinc and Copper
   - Iron (should be used after the first week of treatment).
3. Plasma or albumin for KWO.

IV. Treat of the cause in secondary marasmus

VI. Follow up phase last from 7th week to 26th week

- For feeding to cover catch-up growth
  - High protein diets: eggs, chicken, meat, fish, yogurt, cheese, beans, & lentils.
  - High caloric diets e.g. potatoes, rice
- Providing emotional and sensory stimulation
- Weight gain of 15% is a marker for discharge from hospital

Refeeding syndrome

Definition

- Potentially fatal condition caused by rapid initiation of refeeding after a period of undernutrition (during the 1st week of starting to refeed)
- Hypophosphatemia is the hallmark of this disorder
- Rapid feeding ⇒ hyperinsulinemia ⇒ intra cellular shift of phosphate , potassium ,and magnesium along with salt retention and hyperglycemia

Clinically

- Cardiac: hypotension, arrhythmias
- Respiratory failure
- Neurologic : weakness and paralysis, altered mental status, seizures
- Rhabdomyolysis
- Sudden death

Prevention/treatment

- Give Thiamin 200-300 mg daily oral plus other B complex vitamins
- Start feeding very slow and advance more slowly
- Rehydrate carefully with ReSoMal which has higher potassium & less sodium
- Supplement and or correct levels of phosphate, potassium, calcium & magnesium

Minerals Requirements

	Calcium	Iron	Magnesium	Phosphorus
Daily need	800mg	10-15 mg	100 mg	600 mg
Sources	- Milk, cheese - green vegetables	- Liver, meat - Vegetables, apple	- Milk, meat - cereals, legumes	- Milk, proteins, milk products
Functions	- Bone & teeth - Muscle contraction - Nerve transmission - Blood coagulation - Cardiac action	- Haemoglobin. - Myoglobin. - Oxidative enzymes as catalase & cytochrome oxidase	- Bone & teeth - Conversion of proparathormone to parathormone	- Bone & teeth - Structure of muscles - CHO and fat metabolism
Deficiency	- Rickets - Tetany - Delayed teething	- Iron deficiency anaemia	- Tetany; associated frequencdy with hypocalcemia	- Rickets

Water Soluble Vitamins

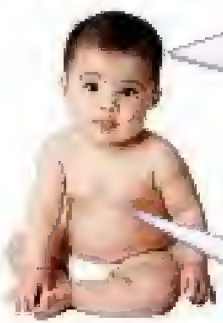
Criteria

- Include vitamins B complex and C
- Not stored in the body so not toxic
- Therapeutic trial→ give dramatic response
- When treating one vitamin deficiency, consider supplying other vitamins as well
- Rich diet: liver , meat ,milk, eggs ,vegetables, cereals ,poultry , fish , whole grains

Vitamin B_1 (Thiamine) deficiency

Beri Beri

1. Early ⇒ Fatigue, insomnia, anorexia

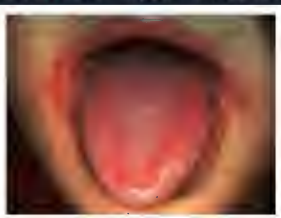


2. Dry Beri Beri
   - Polyneuropathy
   - Dysphonia (recurrent laryngeal nerve paralysis)
   - Ataxia, and psychosis (Wernick's Korsakoff syndrome).

3. Wet Beri Beri → Cardiomyopathy → congestive heart failure with generalized edema

Treatment - B_1 10 mg IM daily (consider supplying other vitamins)

Vitamin B_2 (Riboflavin) deficiency

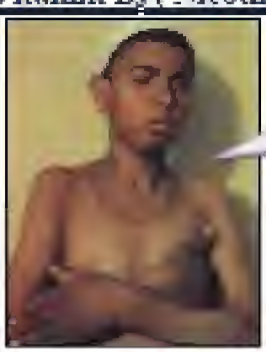


a. Cheilosis , angular stomatitis, glossitis

b. Keratitis and corneal vascularization → Photophobia

Treatment - B_1 10 mg IM daily (consider supplying other vitamins)

Vitamin B_3 (Nicotinic acid, Niacin) deficiency



Pellagra *(pellis = skin, agra = rough)*

1. Dermatitis
   - In sun exposed areas (hands, feet, head & neck).
   - Erythema, scales, crusts & desquamation
   - Sharply demarcated borders

3. Diarrhea - With stomatitis, cheilosis & glossitis
4. Dementia - Apathy.

Treatment - Vitamin B_3 50-300 mg daily
- Avoid maise (poor in tryptophan).

Vitamin B_6 (pyridoxine) Deficiency

1. Infantile convulsions - Why ? B6 is essential for synthesis of inhibitory neurotransmitter; GABA.
   - Nature? Myoclonic type
2. Anemia - Why ? Failure of heme synthesis due to failure of iron utilization.
   - Nature? Microcytic hypochromic.
3. Peripheral neuropathy - In patients on INH therapy
4. Skin - Cheilosis and seborrheic dermatitis

Diagnosis - Therapeutic trial with 100 mg IM in convulsions

Treatment - For pyridoxine dependent child 10-100 mg oral daily
- Diet with rich sources as for vitmain B_3 & soybeans

Vitamin C (Ascorbic acid)

Value - Synthesis of collagen.
- Necessary for folic acid and iron absorption.

Deficiency

1- Bone tenderness mainly in legs → pseudoparalysis.

2- Bleeding: subperiosteal hemorrhages, swollen bleeding gums & purpura.

3- Scorbutic rosary Beads :
- At costo chondral junctions.
- Sharply angular, tender, irregular.
- With sternal depression.

4- Follicular hyperkeratosis(Papular skin)

5- Poor wound healing

6- Pallor due to (hemorrhagic, folic acid deficiency, iron deficiency) anemia

Treatment: Citrus fruits & vitamin C tablets 100-200 mg daily.

Fat Soluble Vitamins

Stored in the body so may be toxic

Vitamin E deficiency

Functions - Cell membrane stabilizer
- Anti oxidant

Causes - Fat malabsorption, malnutrition & prematures

Deficiency - Hemolytic anemia in preterm
- Ataxia.

Vitamin A deficiency

Functions - Retinal function (responsible for night vision)
- Integrity of epithelium (of skin and mucosa)

Deficiency - Night blindness(hard to prove in infancy)
- Eyes → Bitot spots, xerosis, keratomalacia & corneal ulceration.
- Respiratory, gastro intestinal and urinary infection.
- Perifollicular keratosis (Toad s skin)

Toxicity

1. Acute: Due to ingestion of single massive dose.
   - Increased intracranial pressure (vomiting, headache,bulging fontanels)
   - Resolve spontaneously
2. Chronic: Due to large daily doses for weeks to months

   Skin
   - Alopecia
   - Pruritus.
   - Carotenemia (yellow skin)
   - Desquamation of hands and feet

   Bone
   - Craniotabes
   - Metaphyseal Deformities

Self Assessment Case Scenarios

Case 1

A 10-month-old infant presented to the ER with bilateral edema of the lower limbs and pallor. His mother gave a history of recurrent attacks of vomiting and diarrhea. On examination: wt 5.5 kg, pitting edema of both lower limbs, wasting of the muscles of the thigh and ulceration in the buttocks. Abdominal examination revealed enlarged liver 3cm below the costal margins, firm consistency.

a. What is the probable diagnosis?

b. Discuss dietetic management?

Case 2

A 12 months old boy, He was one of twin whose birth weight was 1.700 gm and now he is 4.200 gm. He was given exclusive breast-feeding without any supplementations. The mother was always complaining from insufficient milk in her breast. Examination reveals alert, irritable, crying infant with skin over bone appearance; no other systemic illness

a. What is the underlying disease?

b. What are the possible 4 risk factors for the existing disease?

Case 3

A 1.5 years old female whose mother complains that she is not gaining weight .History reveals that the baby has not been interested in feeding since she was 2 months old ;she got tired easily during breast feeding with marked tachypnea ,tachycardia and sweating. On examination: weight 4 kg.(birth weight was 3 kg) , MAUC 11cm , wasted buttocks but no edema. She is alert, tachypneic , tachycardic ,with soft ejection systolic murmur over pulmonary area and clearly audible second heart sound

a. What type of malnutrition in this case?

b. What is the cause of malnutrition in this case?

c. What are the investigations required to confirm it?

d. What should be lines of treatment for this condition?

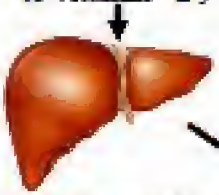
Vitamin D Metabolism

Daily requirement: 400 IU/day if <1 yr old and 600 IU/ day if >1 yr old (mainly for breast milk feeders). For Preterm baby ⇒ 1000 IU/d

Metabolism

❶ There's two forms of vitamin D
- D_2 → ergocalciferol ⇒ plant origin.
- D_3 → cholecalciferol ⇒ animal origin.

❷ Ultra violet rays convert 7- Dehydrocholesterol in the skin to vitamin D_3



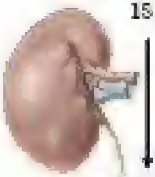
❸ In the liver: Vitamin D_3 is converted to 25 (OH) D_3 by 25 hydroxylase enzyme.

❹ Vit D is absorbed from the upper small intestine with aid of bile salts.

If

- Low serum calcium or phosphate
- High parathyroid hormone level

1 α hydroxylase enzyme is activated.



25 (OH) D_3 → 1, 25 $(OH)_2$ D_3

Active form

⇓

Functions

Via synthesis of transport protein

Normal or high serum calcium

24 hydroxylase enzyme is activated.

25 (OH) D_3 → 24, 25 $(OH)_2$ D_3

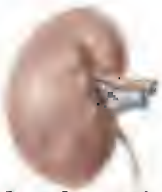
↓

Inactive form

⇐ Ca: Ph ratio 2 : 1

- Enhance Ca. phosphate deposition in bones.

⇐



- ↑ Renal reabsorption of calcium & phosphate

÷

- ↑Intestinal absorption of calcium & phosphate

Vitamin D disorders

Hypervitaminosis D
(Vitamin D intoxication)

Excessive prolonged unmonitored vitamin D intake

Clinical picture

Manifestations are due to hypercalcemia:

System	Manifestations
1. Gastro intestinal	- Vomiting, and constipation - Acute abdominal pain (pancreatitis or peptic ulcer)
2. Renal	- Polyuria, polydipsia and dehydration - Nephrocalcinosis and renal stones
3. Cardiovascular	- Hypertension - Aortic valve stenosis
4. Neurologic	- Lethargy, and coma (pseudotumor cerebri) in severe cases

Prevention

- Monitor serum calcium for cases treated with large doses of vitamin D; if > 11 mg /dl; stop vitamin D

Investigations

- Serum calcium > 11 mg /dl →Suppressed PTH and hypercalciuria
- Hyperphosphatemia
- Elevated levels of 25-D (>150 ng/mL)
- Surprisingly, levels of 1,25-D are usually normal. This may be a result of downregulation of renal 1α-hydroxylase by the combination of low PTH, hyperphosphatemia
- Radiologic: Nephrocalcinosisis often visible on ultrasound or CT scan

Treatment

1. Stop	- Calcium & vitamin D intake - Sun exposure
2. Correct	- Dehydration
3. Enhance urinary calcium loss	- Saline infusion plus Furosemide
4. Reduce calcium absorption	- Prednisone (the best) - Cholestyramin
5. Shift calcium to bones	- Calcitonin
6. Severe hypercalcemia	- Hemodialysis using low or 0 dialysate calcium

Important Notes

❶ Normal serum calcium (Ca) = 9 –11 mg/dl.
Normal serum phosphate (Ph.) = 4.5 – 5.5 mg/dl.
So, Ca: Ph. ratio in blood = 2:1 which is optimal for absorption & mineralization of bones

❷ Production of Ca × phosphate usually constant ≈ **40 – 50** this product is called Holland formula or solubility product.
* If serum phosphate increases → reciprocal decrease in serum Ca occur to keep the formula constant.
* If Holland formula > 80 ⇒ widespread deposition of ca phosphate occur in different tissues (metastatic calcifications) especially in the kidneys & heart.

❸ Serum Ca has 2 forms in balance:
* Non ionized form → inactive
* Inoized form → active form.

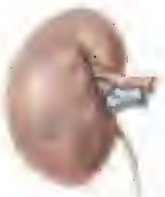
Ionized form

↑ ↑ in acidosis (pH < 7.35) ↓ ↓ in alkalosis (pH > 7.45)

❹ **Parathyroid (Parathormone) hormone** (PTH) is secreted from parathyroid glands
- Main action of PTH is to keep serum calcium constant.
- ↓ Serum Calcium or ↑ Serum phosphate stimulate parathyroids ⇒ ↑ PTH ⇒ *Secondary hyperparathyroidism* (**2ry HPT**).

Actions

• ↑ Ca phosphate mobilization from bones



• ↑ Ca reabsorption & ↑Ph excretion in renal tubules

• ↑Ca & Ph absorption from the intestine

Tetany

Definition: A state of hyper excitability of the central & peripheral nervous system.

Causes

1- Hypocalcemia Due to
- Decreased calcium intake
- Hyperphosphatemia (common in cow milk feeders)
- Magnesium (Mg) deficiency: Mg is essential for parathormone synthesis
- Hypertonic dehydration
- Vitamin D deficiency & hypocalcemic rickets.
- Hypoparathyroidism.
- Acute pancreatitis

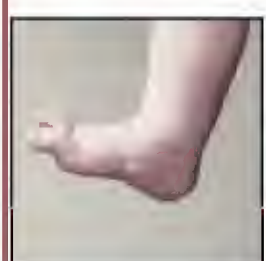
2- Alkalosis (Decreases ionized calcium) Due to
- Loss of HCL due to repeated vomiting.
- Excess alkali intake.
- Barttar syndrome.

3- Hypomagnesemia (N = 1.5 – 2.5 mg/dl).

Clinical picture

A . Latent tetany

With serum calcium 7 – 9 mg/dl; detected by:

			
Chevostek sign Tapping the facial nerve in front of the ear → twitch of the mouth	**Trousseau sign** Inflation of sphygmomanometer cuff over the arm above systolic pressure for 3 min ⇒ *carpal spasm*	**Peroneal sign** Tapping of the peroneal nerve → dorsiflexion + abduction of the foot	**Erb's sign** Motor nerve can be stimulated by low current

B. Manifest Tetany

With serum calcium < 7 mg/dl ; manifested by :

1. Carpo pedal spasm:
   - Flexion of the wrist & metacarpophalangeal joints
   - Extended interphalangeal joints
   - Flexed adducted thumb.
   - Plantar flexion & inversion of the feet
2. Laryngeal spasm (laryngismus stridulous): stridor is afebrile & recurrent.
3. Convulsions: generalized, recurrent,and baby is conscious between attacks

Investigations

For hypocalcemia	For hypomagnesemia	For alkalosis
* Serum Ca (Total & ionized) * Serum inorganic phosphrus * Serum parathyroid hormone.	* Serum magnesium	* Blood gases(pH)

Treatment

A- Hypocalcemic tetany

1. Acute attack

- Immediately relieve hypocalcemia by intravenous calcium
- Dose: 1- 2ml/kg of calcium gluconate 10%
- Slow infusion over 5-10 minutes with cardiac monitoring
- May repeat at 6 hourly until serum calcium level stabilizes.

2. Once symptoms of hypocalcemic tetany have resolved

- Oral calcium 50 mg /kg tapered over 2-6 wk
- Encourage calcium rich diet

3. Vitamin D therapy

- Is started after control of the acute attack
- For hypocalcemia with rickets → oral calcium & vitamin D till healing
- For hypoparathyroidism → oral calcium & active vitamin D

B- For hypomagnesemia

- Mg sulphate 50%
- Dose: 0.2 ml/kg I.V, I.M or oral

C- For alkalosis

- Metabolic alkalosis: Adequate sodium and potassium intake
- Respiratory alkalosis: Re-breath into bag to ↑ $PaCo_2$

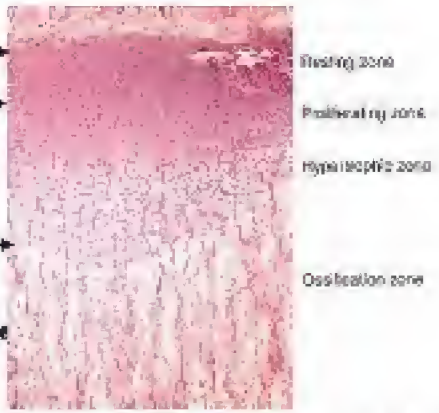
Rickets

Definition

Metabolic bone disease due to failure of mineralization of osteoid tissue of the growing bones due to either:

- Defective intake or metabolism or function of vitamine D.
- Inappropriate calcium / phosphate ratio (usually due to hypophosphatemia, rarely due to calcium deficiency)

Normal bone ossification



- Resting zone: single layer of cartilage cells
- Proliferating zone: Regular avascular cartilage
- Normal zone of provisional calcification → continuous line in ends of long bones radiographs
- Osteoblasts lay osteoid and secrete alkaline phosphtase
- Ossification of osteoid in presence of normal vitamin D & calcium phosphate ratio

In Rickets

- Irregular very vascular *excessive* cartilage(felt clinically)
- Absent zone of provisional calcification → fraying of the ends of the long bones in (radiographs)
- Osteoblasts lay *excessive* osteoid and secrete *excessive* alkaline phosphtase (laboratory)
- Poor ossification of osteoid in *absence* of normal vitamin D *or* calcium phosphate ratio→ weak non rigid bone→ bone yield under pressure → cupping , broadening, deformities and fractures (clinical/radiographs)

So

Rickets is basically suspected clinically and confirmed with both bone radiograph and laboratory

Classification of rickets

Type of rickets	Serum calcium
Calcium deficiency with 2° hyperparathyroidism 1. Nutritional vitamin D deficiency (Infantile rickets) 2. Secondary vitamin D deficiency due to: ○ Malabsorption syndromes (Celiac rickets). ○ Decreased liver 25-hydroxylase activity in chronic liver disease ○ Increased degradation e.g. with anti epileptic drugs. 3. Rickets with chronic renal failure (Renal osteodystrophy) 4. Vitamin D dependent rickets type I 5. Vitamin D dependent rickets type II 6. Calcium deficiency : nutritional , malabsorption or in premature infant	Normal Or Low
Phosphate deficiency without 2° hyperparathyroidism 1. Decreased phosphate intake • Premature infants (rickets of prematurity) 2. Renal phosphate losses e.g. • Familial hypophosphataemia. • Fanconi syndromes • Overproduction of phosphatonin e.g. Tumor-induced rickets	Normal

Causes of rickets other than nutritional rickets are referred to as: Non vitamin D deficiency rickets (or Vitamin D refractory or resistant) as they are not cured with the same dose or form of vitamin D that cures nutritional rickets

(Nelson Textbook of pediatrics)

Vitamin D Deficiency Rickets

Predisposing factors

Season : - Commoner in winter
Age : - Commonest age → 6 months - 24 month.
Growth : - More in rapidly growing infant e.g. twins & preterm.
- Less in infants with arrested growth e.g. PCM & cretinism.

Etiology

A. **Decreased vitamin D intake** due to:

1. Lack of rich sources of vitamin D e.g. egg yolk, meat, fortified milks, fish liver oil.
2. Use of rachitogenic diet with:
   - Poor sources of vitamin D as fresh animal milk ,cereals and carbohydrates.
   - Poor sources of calcium as cereals ,and excess leafy vegetables
   - Inappropriate calcium /phosphate ratio as in fresh animal milk

B. **Lack of access of ultra violet rays to the skin** due to:

1. Lack of sun exposure
2. Poor sun exposure through glass windows, clouds & dust.
3. Excessive wrappings of the infants.
4. Poor penetration in dark skinned infants

Clinical picture

I. Early Rickets

1- Anorexia, irritability, & sweating of forehead

2- Craniotabes

- Skull bones yield under pressure →
  Ping - pong or egg shell crackling sensation.
- Due to thinning of inner table of the skull
- Disappear by the end of 1st year.
- Detected by pressing over occipital or parietal bone

3- Rachitic rosaries: palpable enlargement of costochondral junctions (excess

II. Advanced Rickets

i. Skeletal Changes

1. Head

- Large head
- Large anterior fontanel (delayed closure).
- Asymmetric skull; may be box shaped

- Frontal & parietal bones bossing due to excess osteoid
- Depressed nasal bridge
- Delayed teething, dental caries

2. Chest

- Rachitic rosaries
  - Visible & Palpable.
  - Rounded, Regular, Non tender

- Longitudinal sulcus → lateral to the rosaries
- Harrison sulcus → transverse groove along the costal insertion of the diaphragm
- Chest deformities:
  * Pigeon chest → sternum & adjacent cartilages project forwards.
  * Funnel chest → depression of the sternum & flaring out of the lower ribs.

3. Vertebral column : there may be

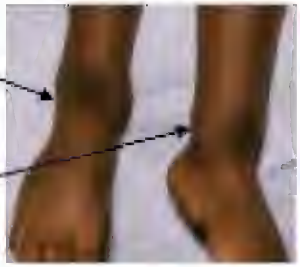
a. Kyphosis: in dorsolumbar region

- Smooth.
- Apparent on sitting, disappear by lifting.
- With compensatory lumbar lordosis

b. Scoliosis: lateral curvature of the spine

4. Extremities

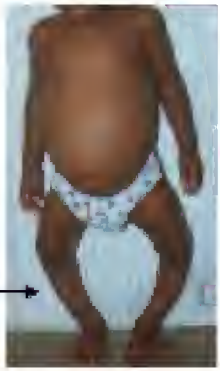
a. Broadening of epiphysis of long bones especially at wrist & ankles.



b. Marfan sign: transverse groove over the medial maleolus due to unequal growth of the two ossific centers.

c. Deformities: Due to weight bearing on the soft bones;

* Crawling infants:
  - Bowing of forearm
  - Anterolateral curvature of femurs
  - Anteroposterior curvature of legs
* Walking child:
  - Bow legs(Genu varus)
  - Knock knees (Genu valgum)
  - Overextended knees(Genu recurvatum)



ii. Non Skeletal Manifestations

Manifestations:

1- Delayed motor milestones.

2- Abdominal distension (pot belly abdomen) ; with or without umbilical hernia

3- Ptosis of the liver & the spleen (also due to chest deformities).

4- Constipation → due to intestinal hypotonia.

Etiology: - Hypotonia of skeletal muscles (due to hypophosphatemia)

- Laxity of ligaments

Complications

1- Respiratory infections & atelectasis due to:

a- Limited chest expansion.

b- Hypotonia of respiratory muscles → weak cough reflex.

2- Gastroenteritis due to intestinal hypotonia → stasis → 2ry bacterial overgrowth.

3- Tetany : may occur in rickets with hypocalcaemia

4- Skeletal deformities: - Mild and early managed cases → reversible.
- Advanced and neglected cases → permanent.

5- Disproportionate short stature (Rachitic dwarfism)→ due to deformities of spine, pelvis & limbs

6- Iron deficiency anemia is a common association (Von-Jack anemia = anemia , rickets , lymphadenopathy and splenomegaly)

Investigations

I. Biochemical

- Serum calcium is normal, but may be low (normal = 9 – 11 mg/dl).
- Serum inorganic phosphrus (Ph.) is low (normal value = 4.5 – 6.5 mg/dl).
- Serum Calcium × Phosphate product is low (less than 30).
- Serum alkaline phosphatase enzyme (Alk. Phos.):
  - High
  - The most sensitive indicator of rachitic activity; due to osteoblastic activity
  - Return to normal after complete healing of rickets.
- Serum Parathyroid hormone (PTH) → high.
- Serum 25 (OH) D_3 → low
- Serum 1.25 $(OH)_2$ D_3 → low in severe vitamin D deficiency

Explanation: ↓ 1,25 $(OH)_2$ D_3 →↓ calcium absorption → serum calcium tend to be low → ↑ PTH → ↑ calcium & ph. mobilization from bones + ↑ ph. loss in urine → normalized serum calcium + ↓ serum ph.

However hypocalcemia (and may be tetany) may occur with:

1- Failure of 2^{ry} hyperparathyroidism to occur.

2- In advanced cases with depletion of bone calcium.

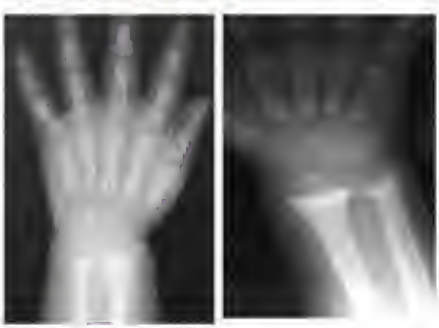
3- Shock therapy → ↑↑↑ deposition of calcium Ph. in bone on the expense of serum calcium which may fall below normal.

II. Radiologic: by X-ray at lower ends of long bones especially wrist due to easy access , rapid growth and soft tissue around is thin.

a. Active rickets

The lower ends show

- Broadening ; widening of the distal end of the metaphysis
- Cupping or concavity ; metaphysis changes from a convex or flat surface to a more concave surface
- Metaphysis loses its sharp border (Fraying)
- Wide joint space



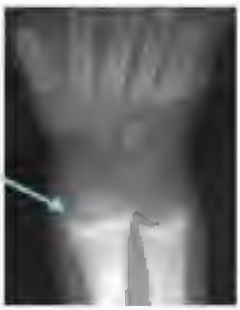
Normal wrist Rachitic wrist

The shaft shows

- Rarefaction → ↓ bone density
- May be green stick fracture.
- May be deformities

b. **Healing rickets**

- Usually seen 2 weeks of vitamin D therapy
- The lower ends shows white concave continuous line at ZPC
- Less evident features of rickets



c. **Healed rickets**

- Usually seen 4 - 6 weeks of vitamin D therapy
- The lower ends show straight continuous line at ZPC.
- No features of active rickets.

Differential diagnosis from other causes of :

1. Non vitamin D deficiency rickets
2. Delayed motor milestones e.g. Inability to walk
3. Craniotabes which may occur in:
   - Premature→ disappear by the 3rd month
   - Hydrocephalus→ weakness affect all bones
   - Osteogenesis imperfecta→ weakness since birth
   - Congenital syphilis.
4. Pott's disease (T.B of spine): - Kyphosis is angular & persistent.
   - X-ray and CT spine is diagnostic.
5. Rosary beads:
   a. Scorbutic Rosaries: Due to deficient collagen → subperiosteal hemorrhage
   Criteria: - At costo chondral junctions.
   - Angular, tender, irregular.
   - With sternal depression.
   - Associated with other clinical features of scurvy
   c. False Rosaries in marasmus : Prominent normal costochondoral junctions

N.B. Atrophic rickets

- Rickets in non growing bones as in protein calorie malnutrition
- Absent osteoid overgrowth signs i.e. No bossing , wrist or ankle broadening , rachitic rosaries nor Marfan sign.
- Other signs of rickets are present e.g. wide fontanels, hypotonia,.....

Treatment

1. Prevention

a. Vitamin D supplement usually as daily multivitamin

Dose: - For less than 1 year → 400 IU/day mainly for Breast feeders

- For above 1 year → 600 IU/day

b. Advice for:

- Exposure of pregnant mothers and infants to sunlight
- Diet with adequate calcium and phosphorus(formula, milk , dairy products)
- Vitamin D and calcium supplement for pregnant and lactating mothers

2. Curative

a. Vitamin D_3:

* Oral : 2000 – 5000 IU/day for 4 - 6 weeks

* Stoss (Shock) therapy :

- 300.000- 600.000 IU IM or oral for 2-4 doses over 1day
- Indicated if compliance is uncertain

Either strategy should be followed by daily vitamin D intake maintenance

b. Advice parents for:

- Advice about Diet and sunlight as before
- Avoid weight bearing in infants during active rickets.

c. Treat complications:

* Tetany

* Deformities: osteotomy and reconstruction if severe and persistent.

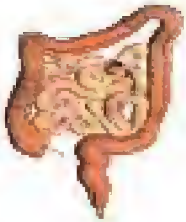
After 4- 6 weeks of treatment: Look for criteria of improvement:

1. Radiologic : Appearance of zone of provisional calcification is the earliest finding.
2. Laboratory : Normalization of alkaline phosphatase indicates complete healing
3. Clinical: Improved muscle tone but skeletal manifestations may take a longer time (Some skeletal signs may persist as large head , severe deformities, pigeon chest)

Decision: Reduce vitamin D dose to the normal daily requirement (to avoid toxicity)

Other Hypocalcemic Rickets

1. Rickets with malabsorption



- Clinical and lab features of malabsorption

+

- Clinical , lab and radiologic features of infantile rickets

Treatment: Treat malabsorption syndrome + 25 OH D3 or calcitriol (Better absorption) or Parenteral Vit D
The dose is adjusted based on monitoring of serum levels of 25-D

2. Rickets with chronic liver disease

- Clinical features of chronic liver disease→ jaundice, bleeding, edema
- Lab features of chronic liver disease → Raised bilirubin , liver enzymes , prolonged PT , low albumin

+

- Clinical , lab and radiologic features of infantile rickets

Treatment : Treat chronic liver disease + 25 OH D3

3. Rickets with anti epileptic drugs

- Prolonged anti epileptic medicines (phenytoin , phenobarbitone or carbamazepine) → enzyme inducers → inactivation of 25 (OH) D_3
- Poor sun exposure or poor diet in neurologically disabled

+

- Clinical , lab and radiologic features of infantile rickets

Treatment: Oral calcium+ Sun exposure + 25 OH D3
Prevented by extra dose of vit D for all susceptible epileptics

4. Vitamin D dependent rickets type I

- Autosomal recessive defect in 1 α hydroxylase enzyme
- Clinical , lab and radiologic features of infantile rickets

But

- Develop early in life
- Serum vitamin D: Normal 25 OH D3 / Low 1,25 $(OH)_2$ D3

Treatment: Oral calcium + 1,25 $(OH)_2$ D3 (R/Calcitriol)
Monitor urinary calcium excretion, with a target of <4 mg/kg/day

5. Vitamin D Dependent Rickets Type II

- Autosomal recessive end organ resistance to 1.25 $(OH)_2$ D_3
- Clinical , lab and radiologic features of infantile rickets

But

- Develop very early in life
- Serum vitamin D: Normal 25 OH D3 / High 1,25 $(OH)_2$ D3
- Associated with short stature and alopecia totalis (severe)

Treatment: Oral calcium+ Calcitriol high dose may be of value

A trial period of 3-6 months with this regimen is initiated

Monitor urinary calcium excretion, with a target of <4 mg/kg/day

6. Renal Osteodystrophy (ROD) (Renal Glomerular Rickets)

Pathogenesis

Chronic renal failure

- Phosphate retention
- ↓ 1 α hydroxylase → ↓ 1.25 $(OH)_2$ D_3 synthesis
- Metabolic acidosis

↓ serum calcium

Impaired bone mineralization

Secondary hyperparathyroidism (2ry HPT)

Increased bone resorption(↑ Calcium & phosphate mobilization form bones)

More phosphate retention (vicious circle is settled)

Clinical picture

a. Features of chronic renal failure(anorexia ,anemia, growth failure, hypertension, …)

b. General features of rickets but:

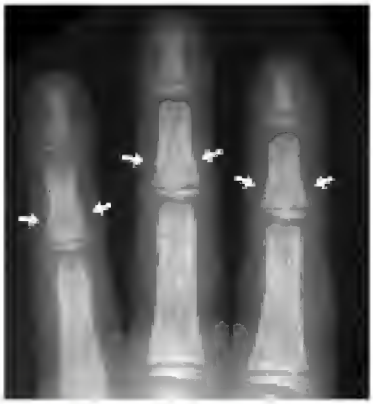
- Deformities & fractures are very common due to combined effect of rickets & secondary hyperparathyriodism.
- Tetany is rare → as metabolic acidosis ↑↑ ionized Ca
- Bone pain and muscle weakness in older children.

Investigations

1- Biochemical:

Ca	Ph.	PTH	ALK phos.	25 $(OH)_2$ D_3	1.25 $(OH)_2$ D_3
Normal or ↓	↑↑	↑↑	↑	Normal	↓

- Evidence of renal failure (↑urea & creatinine),and anemia
- Urinary phosphate is low unlike other types of rickets



2- Radiologic

* **General radiological features**
* Evidence of secondary hyperparathyriodism:
  - Subperiosteal erosions of bones
  - May be bone cysts ⇒ osteitis fibrosa cystica.

Management

A- Treatment of CRF → conservative treatment with or without dialysis.

B- Treatment of ROD in the following steps guided by target level of PTH as decided by stage of renal failure:

1. Low phosphate diet (consult dietician).
2. Oral phosphate binders → Calcium carbonate (calcimate) or
   → Calcium acetate or
   → Non calcium based binders (sevelamer; Renagel)
3. Correct chronic metabolic acidosis by sodium bicarbonate tablets
4. Oral One alpha [1 α (OH) D_3] or calcitriol

↓

5. Calcimemtic drugs e.g. Cinacalcet can suppress hyperparathyroidism without inducing hypercalcemia

↓

6. Partial parathyroidecomy for persistent hyperparathyroidism.

N.B. Congenital rickets

- Due to severe maternal vitamin D during pregnancy
- Presentation: a newborn with :
  a- Classic rachitic changes
  b- Hypocalcemic tetany
  c- Intra uterine growth retardation
- Prevented by adequate prenatal sun exposure and vitamin D supply

N.B. Calcium deficiency rickets

Tend to present later than Vit D deficiency rickets ; namely after weaning from breast feeding. May be associated with Vit D deficiency
Treated by supplemental calcium according to age

Hypophosphatemic Rickets

Renal Tubular Rickets

Rickets develop with renal tubular disorders due to either.

- Phosphaturia →↓ serum phosphate → serum Ca: Ph ratio become inappropriate for mineralization.
- Metabolic acidosis →↑ bone resorption.

Types of renal tubular rickets:

1- Familial hypophosphatemia
2- Fanconi syndromes:
   a. Primary
   b. Secondary
      - Cystinosis (Lignac syndrome)
      - Oculo-cerebro-renal (Lowe's syndrome)
      - Galactosemia.
      - Out dated tetracycline , mercury poisoning
3- Renal tubular acidosis

1- Familial hypophosphatemia	2- Fanconi syndrome (Idiopathic type)
Etiology Sex linked dominant disorder Characterized by decrease renal tubular reabsorption of phosphate → loss of phosphate in urine	Autosomal recessive disorder due to multiple defects in proximal renal tubules with ↓ urinary reabsorption of phosphate, bicarbonate & amino acids and may be potassium & glucose→ all are lost in urine
Clinical picture - Rickets appear during the 2nd year of life especially bow legs with waddling gait and short stature. - Delayed teething and tooth abscesses - No evident rosaries , muscle weakness nor tetany	- Rickets (due to phosphaturia , acidosis) - Vomiting (due to acidosis) & constipation - Polyuria and polydipsia - Episodes of dehydration and fever - Muscle weakness - Growth retardation - May be renal stones (uric acid)
Laboratory • ↓ Ph. • Normal Calcium • No 2ry HPT • ↑ Alk. Phosphatase Others: Phosphaturia	• ↑ urinary Ph., bicarbonate & amino acids (may be potassium & glucose) • Metabolic acidosis

Treatment

1. Oral phosphate 1 – 3 gm/day divided into 5 doses
2. Vitamin D:

Value :- Complete bone healing
- Offset 2ry HPT which usually accompany phosphate therapy.

Use: - Calcitriol (Calcitriol exerts negative feedback with PTH)

3. Oral bicarbonate for metabolic acidosis
4. Oral potassium for hypokalemia
5. Free access to water: 2-6 liters per day

(Nelson text book of pediatrics)

3- Lignac syndrome (cystinosis)

- Autosomal recessive intra celluar storage disease characterized by deposits of cystine in lysosomes of liver, spleen, bone marrow, cornea & renal tubules → Fanconi like.

- Clinical and laboratory features of Fanconi

Plus

- Blond hair and fair skin
- Photophobia
- Untreated cases end in chronic renal failure by 10 years
- Elevated leucocyte cystine level
- Detect cystine crystals in cornea by slit lamp

- Treatment: as Fanconi & mercaptamine (cysteamine) oral & eye drops.

4- Lowe's (oculo – cerebro – renal) syndrome

- Sex linked recessive disorder of eyes, cerebral cortex & renal tubules → Fanconi like

- Clinical and laboratory features of Fanconi

Plus

- Eye → cataract & congenital glaucoma (Buphthalmos).
- CNS → mental retardation & hypotonia

- Treatment: as Fanconi & treat associations

5- Renal tubular acidosis

- Mainly proximal renal tubules defect → bicarbonaturia → Metabolic acidosis
- Clinical picture, investigation & treatment → as Fanconi

Conditions Resembling Rickets

1- Hypophosphatasia

* Due to : Decreased serum alkaline phosphatase enzyme
* Inheritance : Autosomal recessive disorders
* There may be ↑ serum calcium
* Treatment : No specific treatment ; some cases may benefit from fresh plasma

2- Metaphyseal dysplasia

* Inheritance : - Autosomal dominant disorders
* Forms : - Jansen type
  - Schmidt type
* Clinical picture : - Short stature.
  - Bow legs with waddling gait.

Self Assessment Case Scenarios

Case 4

A 12 months old boy, presented to ER with severe respiratory distress. On examination he has severe stridor with suprasternal and substernal retractions, cyanosis, and disturbed conscious level. No history suggestive of foreign body inhalation .Further examination reveals broad wrists and ankles, plantar flexion of feet and abnormal posture of both hands.

a. What is the complication and the underlying disease?

b. What should be lines of treatment of presenting condition?

Case 5

A 14-month-old child has lower-extremity bowing, a waddling gait, genu varum, and is at the 5th percentile for height. Laboratory data include normal serum calcium, moderately low serum phosphate, and elevated serum alkaline phosphatase levels, hyperphosphaturia, and normal parathyroid levels.

What is the most likely diagnosis?

A. Fanconi syndrome

B. Genetic primary hypophosphatemia

C. Malabsorption of vitamin D

D. Phosphate malabsorption

E. Renal osteodystrophy

Case 6

5-year-old girl is somewhat short and has mild leg bowing. Her medical history is significant only for well-controlled seizure disorder. Serum calcium, phosphorus, and alkaline phosphatase levels and urinary amino acid concentration are normal. A bone age is notable for abnormal distal radius and ulna mineralization.

Which of the following is the most likely diagnosis?

A. Malabsorption syndrome

B. Fanconi syndrome

C. Genetic primary hypophosphatemia

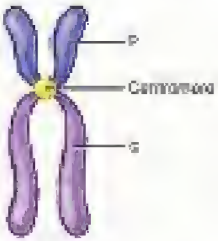
D. Rickets associated with anticonvulsive drug use

E. Metaphyseal dysplasia

Genetic disorders

Basics of Genetics

Chromosome structure



- Each chromosome is composed of 2 chromatides
- The 2 chromatides are connected to at the centromere
- Each chromosome has 2 short arms (p) & 2 long arms (q)
- Each chromatide is composed of DNA in a protein framework.

Chromosomal number

1. **In somatic cells** : 46 chromosomes (i.e. diploid number) ; 44 autosomes& 2 sex chromosomes; X X in females & X Y in males
2. **In germ cells** : 23 chromosomes (i.e. haploid number); 22 autosomes & One sex chromosome(X in ovum and X or Y in sperm)

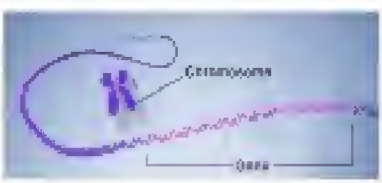
Mitotic Division

- Occur in all cells excepts CNS cells for renewal of cells & ↑number of cells
- Steps : Chromosomes arranged along the equatorial plane→ Spindle protein fibers radiate from the centrioles to the centromeres →Each chromosome divide longitudinally into 2 daughter chromatides →Each set of chromatids moves to each pole of the cell →2 daughter cells will form each contain 46 chromosomes (chromatids)

Meiotic Division

- Occur only in gonads for production of gametes (ova & sperms)
- Each gamete has a reduction of chromosomal number from 46 to 23
- Steps: Homologous chromosomes pair longitudinally (crossing over may occurs between 2 homologous chromatides) → Spindle connects centrioles to the centromeres→ Homologous chromosomes separate randomly to each pole of the cell→ production of 2 cells; each has haploid number of chromosomes→ frequent mitosis follow on

Structure of the gene



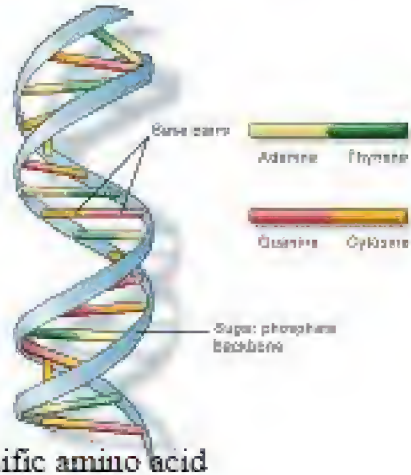
- Part of DNA that code for synthesis of single polypeptide chain.
- Every trait (character or feature) is determined usually by 2 genes; one from each parent.
- If both genes are similar → Homozygous (e.g. AA or aa)
- If both genes are different → Heterozygous (e.g. A a)
  - **Dominant gene** : Expresses itself whether in homozygous or heterozygous state
  - **Recessive gene** : Expresses itself only when homozygous

Each DNA is composed of

a- Sugar (deoxyribose) & phosphate backbone.

b- Nitrogenous bases:

- Pyrimidines : cytosine (C)&thymidine (T)
- Purines : adenine (A) & guanine (G).
  - * A always pairs with T.
  - * C always pairs with G.

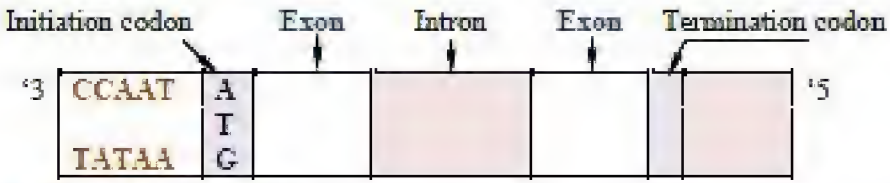


- Nucleotide is a unit of :
  - One deoxyribose
  - One phosphate group
  - One nitrogenous base
- Each 3 successive nucleotides code for a specific amino acid

Gene Expression

Human gene is composed of

- **Exons:** Functional unit of gene sequences; coding for protein synthesis.
- **Introns:** Non coding DNA sequences of unknown function.
- **Initiation codon:** Specific sequence that determines initiation of protein synthesis.
- **Termination codon:** Specific sequences (TAA, TAG or TGA) which determine the end of transcription.
- **TATAA and CCAAT boxes:** Special sequences with unknown function, but may direct the enzymes for initiation sites.



Control of gene expression

- Different cells have special functions due to different genes expression
- This can be achieved by methylation theory which states that: Parts of the gene which is methylated tend to be non-functioning and non-methylated parts tend to be functioning.

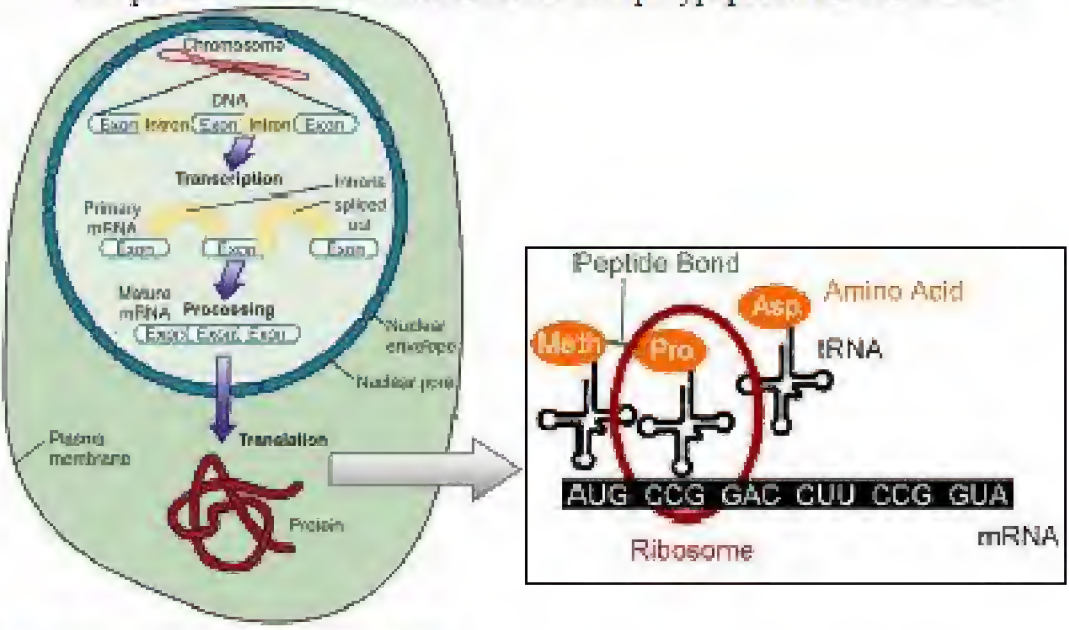
Types of DNA

- Non repetitive (unique) DNA - Code for mRNA
  - Involved in protein synthesis
- Repetitive DNA - Repeated DNA sequences
  - Not coding for genes
- Mitochondrial DNA - Circular , maternally inherited
  - 2-10 copies of double stranded DNA

DNA functions

A. Protein synthesis (*see the figure below*)

1. **Transcription**: synthesis of mRNA strand with the same sequence of DNA strand.
2. **Processing**: the non coding segments (introns) of mRNA are removed and the remaining parts are joined together to form a functional mRNA
3. **Translation**
   - mRNA leave the nucleus & attach to the ribosomes in the cytoplasm
   - When the ribosomal RNA comes in contact with that codon the tRNA with specific anticodon complementary to it comes in place, leaving the specific amino acid carried on it.
   - The mRNA moves and brings another codon in contact with ribosome.
   - Another tRNA comes in place and its amino acid attach to the first amino acid.
   - The process will continue until the whole polypeptide chain is formed



B. DNA replication (Duplication)

DNA can replicate itself (i.e. copy itself)

- **Aim**
  - DNA repair itself to replace a missed or broken segments after exposure to injurious agents e.g. irradiation
  - Formation of a complementary strand during cell division
- **How**

DNA helix split → form two single strands → pairing of the new complementary bases

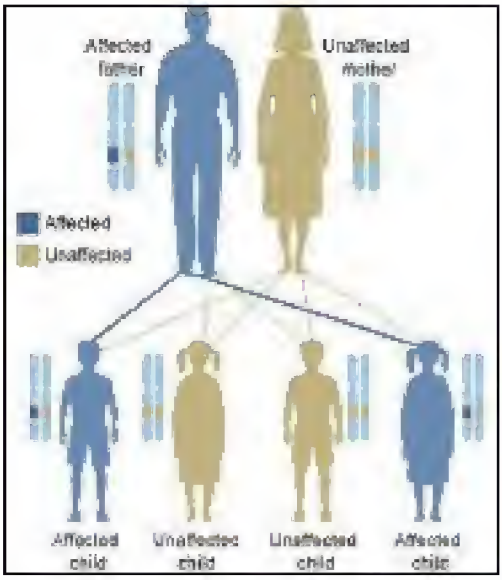
Modes of inheritance

i. Mendelian inheritance

1. Autosomal dominant (AD)

Criteria

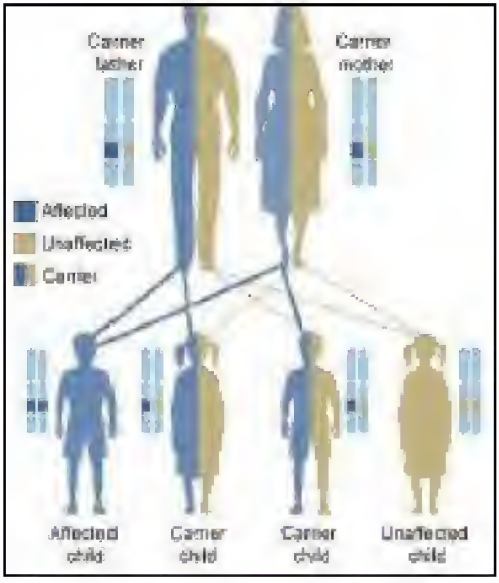
- The trait manifest in homozygos or heterozygous state
- Affected person has an affected parent (vertical transmission)
- Disease is transmitted from the affected person to ½ of his offspring
- Disease appear in all generations
- New mutation is common
- Examples
  - Spherocytosis
  - Von Willbrand disease



2. Autosomal recessive (AR)

Criteria

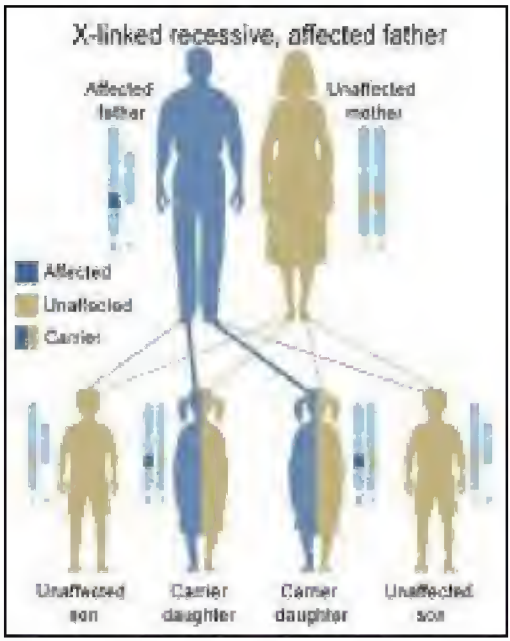
- The trait manifests only in homozygous state
- Both parents are carriers→ Consanguious marriage increase the incidence
- Offspring: ¼ free , ¼ affected and ½ are carriers
- Examples
  - Thalassemia
  - Inborn errors of metabolism e.g. phenyleketonuria, albinism



3. Sex- linked recessive (XR)

Criteria

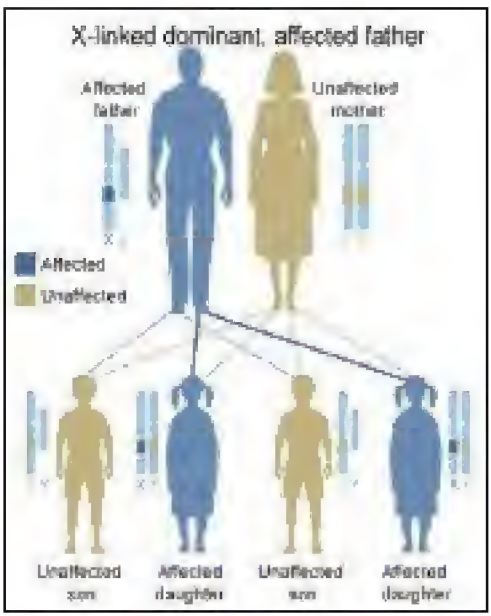
- Affect all males carrying affected gene while in females it appear only if homozygous
- Female carriers have ½ of her sons affected and ½ of her females carriers
- Affected father have all his females carriers but there is no father - son transmission
- Females may be affected if: affected male marry carrier female or female with only one copy of x chromosome (Turner) or due to Lyonisation(random inactivation of the sound X chromosome leaving the other X chromosome unopposed).
- Examples:
  - G6PD deficiency
  - Heamophelia A



4. Sex linked dominant (XD)

Criteria

- All persons -whether male or female- carrying the affected gene will express the trait
- Affected father transmit the trait to all daughters but never to this sons
- Affected mother transmit the trait to ½ of her offspring whether males or females
- Example:
  Familial hypophosphataemia



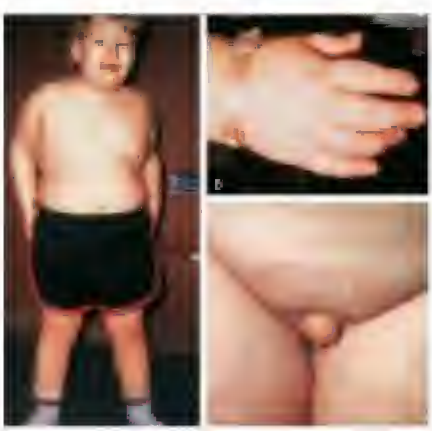
ii. Non Mendelian modes of inheritance

A) Multifactorial inheritance

* Caused by a combination of inherited and environmental factors
* Risk of recurrence is increased when multiple family members are affected and when the disease is severe
* Examples: - Cleft lip and cleft palate
  - Congenital pyloric stenosis
  - Diabetes mellitus

B) Non traditional modes of inheritance

1. **Mitochondrial DNA mutations** e.g. mitochondrial disorders
   - Criteria
   - Maternally inherited but affect both sexes
   - Common manifestations: - Hypotonia, seizures, developmental delay
     - Deafness and impaired vision
     - Cardiomyopathy, diabetes mellitus
2. **Genomic imprinting**
   - It is functional inactivation of a gene depending on the parent of origin
   - Example: Prader Willi Syndrome/ Angelman Syndrome
     - Both syndromes are associated with loss of the chromosomal region 15q11-13
     - Paternal inheritance of a deletion of this region is associated with Prader Willi Syndrome
     - Maternal inheritance of the same deletion is associated with Angelman Syndrome

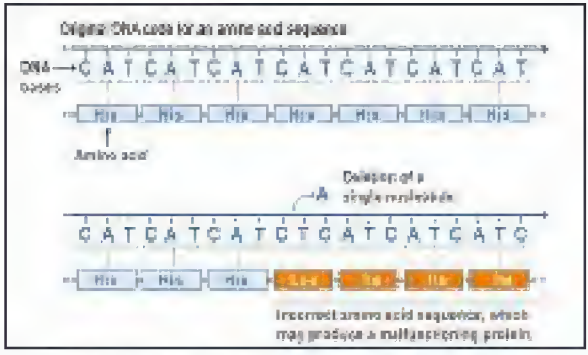
Prader Willi Syndrome	Angelman Syndrome
	
Mental retardation, hypotonia, hypogonadism, obesity, slender fingers and short stature	Mental retardation, gelastic seizures, fair skin and hair and global developmental delay

Mutation

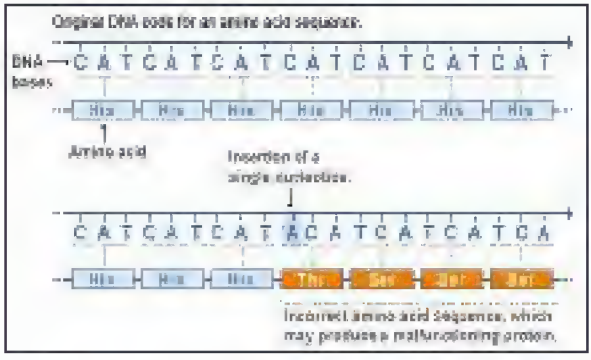
Definition: A change in DNA sequence.

Types

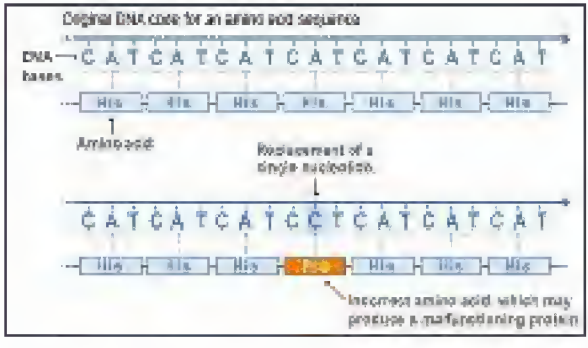
1. **Deletion mutation**
   One nucleotide is deleted from the DNA code, changing the amino acid sequence that follows



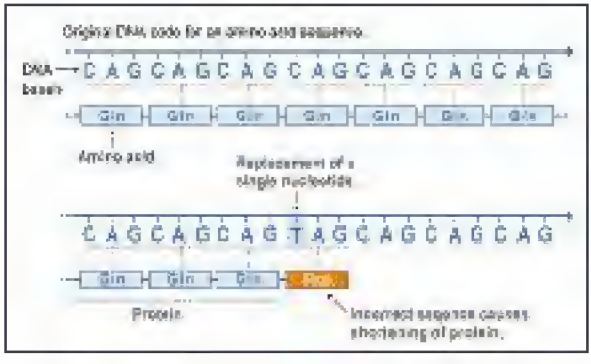
2. **Insertion mutation**
   One nucleotide is added in the DNA code, changing the amino acid sequence that follows



3. **Missense mutation**
   A nucleotide is replaced by another one in the genetic code, introducing an incorrect amino acid into the protein sequence

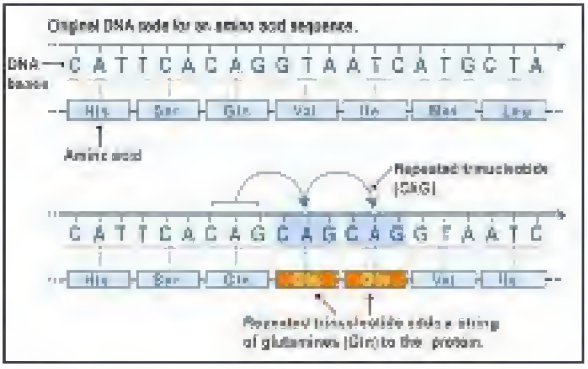


4. **Non sense mutation**
   A nucleotide is replaced by another in the DNA code, signaling the cell to shorten the protein



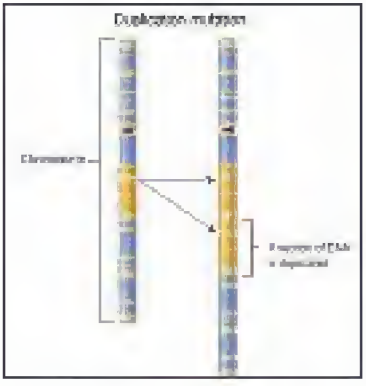
5. Tandem repeat mutations

- A repeated trinucleotide sequence adds a series of an amino acid to the resulting protein
- This expansion leads to gene
- Inactivation which increase with increase size of the repeats
- The disease increase in severity in subsequent generations
- Examples:
  - Fragile X syndrome (CGG nucleotide repeats)
  - Friedreich ataxia (GAA nucleotide repeats)



6. Duplication

A section of DNA is accidentally duplicated when a chromosome is copied



Outcomes of mutations

- Silent mutation
- Gain of function mutation:
  - Over expression of the gene product
  - Most are autosomal dominant disorders
- Loss of function mutations:
  - Under expression of gene→ gene product is insufficient for normal functions
  - Most are autosomal recessive disorders.
- Mutations confer a novel property on the produced protein without altering the normal function e.g. sickle cell disease.
- Oncogenes: mutations affecting normal regulators of cellular proliferations causing cancer.

Diagnosis of mutation

By specific DNA probes using:

- Florescent In Situ Hybridization (FISH) technique or
- Polymerase Chain Reaction (PCR)

Chromosomal Analysis(Karyotyping)

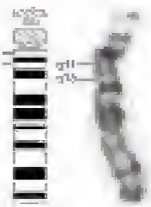
Karyotyping: Systematic arrangement of the chromosomes of a single prepared cell in pairs (according to the length) by photography

Preparation of study cells; cells can be obtained from:

1. Peripheral blood lymphocytes: Used for routine karyotyping.
2. Bone marrow: For rapid analysis and in leukemia.
3. Skin fibroblasts: In suspected mosaicism or if blood is not available
4. Amniotic fluid cells: Diagnose chromosomal anomalies in the 2nd trimester.
5. Chorionic villous sampling (CVS): Diagnose chromosomal anomalies in the 1st trimester (at 10-12 weeks).
6. Fetal cells in maternal blood analysis using FISH technique (Recent)

Techniques

1. G-banding
   * Chromosomes are stained in metaphase using Trypsin/Giemsa stain → examined under light microscope
   * Chromosomes appear as dark bands alternating with light bands.
2. High resolution banding
   * As G-Banding but each band is subdivided into sub bands



Normal karyotyping

* Female: 46, XX
* Male : 46, XY

Indications of karyotyping

1. In neonate	- Confirm clinical diagnosis. - Dysmorphic features. - Ambiguous genitalia. - Major congenital malformations
2. In childhood	- Females with unexplained short stature or growth retardation. - Mental retardation of unknown origin. - Delayed puberty.
3. In adults	- Parents of child with chromosomal anomaly - Parents with 2 or more abortions of unknown cause. - Amniocentesis for mother with previous child with congenital anomalies and mothers > 35 years old.

Classification of Chromosomes Chromosomes are classified regarding:

1- Size: short, medium sized, long.

2- Position of centromere:

* Metacentric → central centromere (p arm and q arm of almost equal size)
* Submetacentric → (p arm shorter than q arm).
* Acrocentric → centromere is close to one end (very short p, very long q)

Denver classification of chromosomes: (7 groups)

A 1, 2, 3 - Large - Metacentric	B 4, 5 - Large - Submetacentric	C 6 → 12 & X - Medium - Submetacentric	
D 13, 14, 15 - Medium - Acrocentric	E 16, 17, 18 - Short - submetacentric	F 19, 20 - Short. - Metacentric	G 21, 22, Y - Short. - Acrocentric

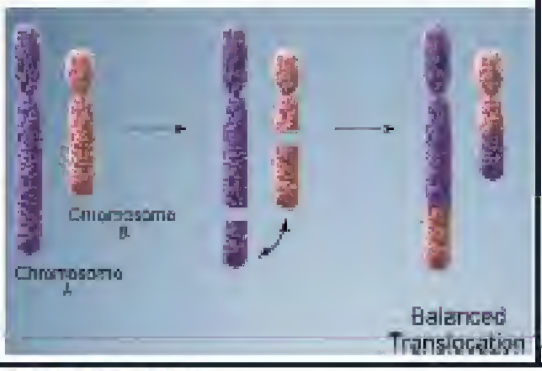
Chromosomal anomalies

A. Abnormalities of chromosome structure

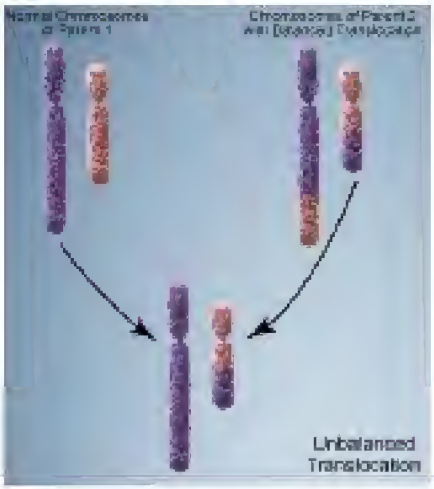
1. Translocation (t)

Part of chromosome is broken and joined to another chromosome

a. **Balanced** : Pieces of chromosomes are rearranged but no genetic material is gained or lost in the cell



b. **Unbalanced** : occurs when a child inherits a chromosome with extra or missing genetic material from a parent with a balanced translocation

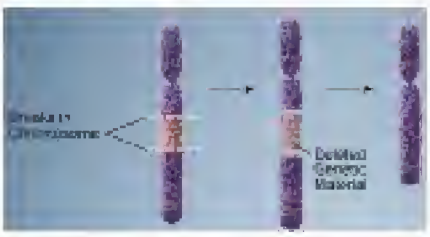


2. Deletion (del)

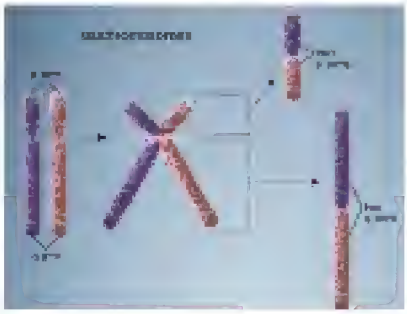
* Part of the chromosome is broken & lost ⇒ gene loss.
* Example:

Cri du chat syndrome (deletion chr. 5 p):

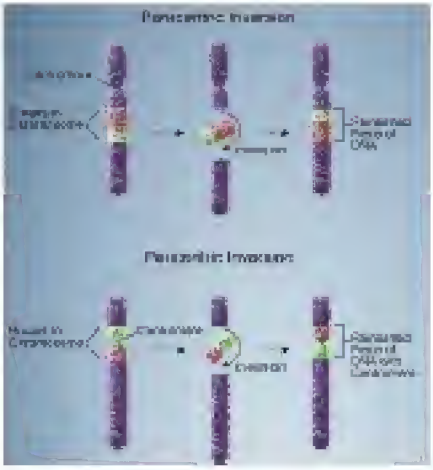
- Mental retardation & miCrocephaly
- Cry like cats
- Congenital heart disease



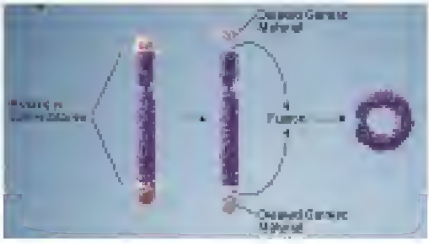
3. **Isochromosome** (i)
   - Transverse division of the chromosome instead of longitudinal division
   - Resulting in 2 chromosomes with two identical arms, either two short (p) arms or two long (q) arms



4. **Inversion** (inv)
   - Occur when a chromosome breaks in two places and the resulting piece of DNA is reversed and re-inserted into the chromosome.
   - Inversions that involve the centromere are called pericentric inversions
   - Inversions that do not involve the centromere are called paracentric inversions

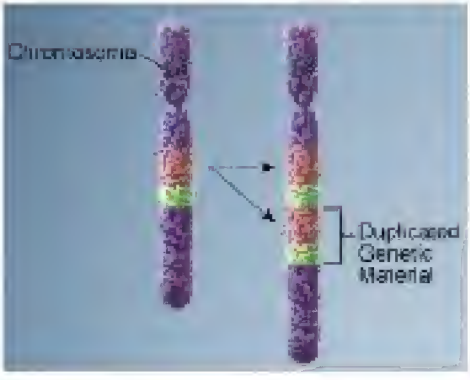


5. **Ring chromosome** (r)
   - Breaks at both ends of a chromosome with subsequent end to end rejoining
   - Often cause growth retardation and mental handicap.



6. **Duplication** (dup)

* A duplication occurs when part of a chromosome is copied (duplicated) abnormally, resulting in extra genetic material from the duplicated segment

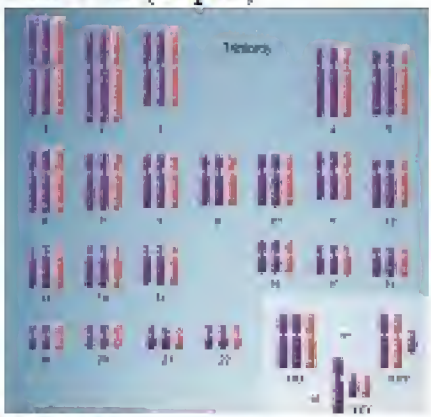


B. Abnormalities of chromosome number (Numerical anomalies)

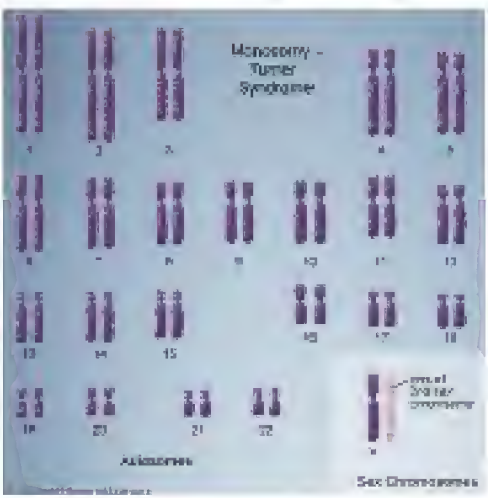
1. **Euploidy** cells containing normal number of chromosome(23 pair)
2. **Polyploidy**

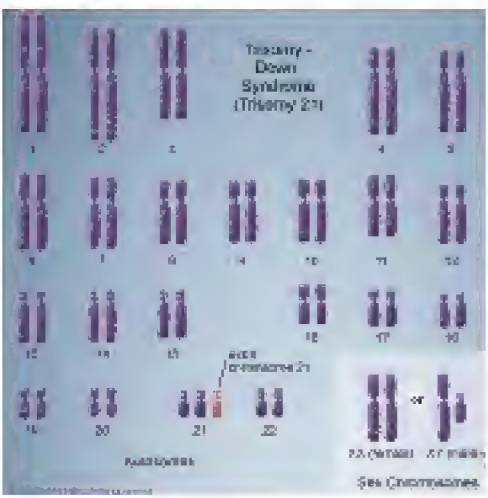
   Extra whole sets of chromosomes:

   e.g. **Triploidy** 69, XXX; (lethal)



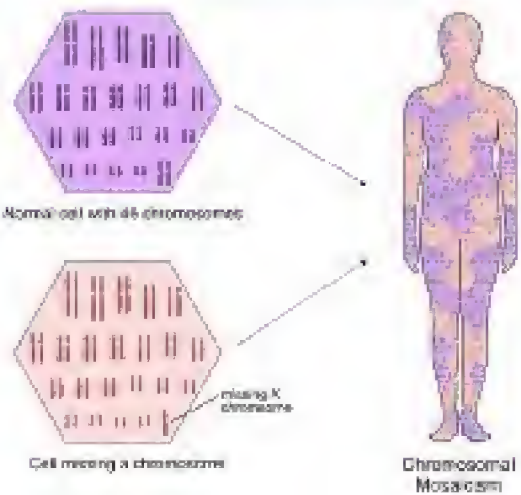
3. **Aneuploidy**: Missing or extra individual chromosomes
   a. **Monosomy**: only one copy of a particular chromosome (most are aborted).
   b. **Trisomy**: three copies of a particular chromosome





4. **Mosiacism**

- The presence of two or more different chromosome counts in different cells of the same individual
- Karyotyping of skin fibroblast help establish diagnosis as, unlike most cells, it withstand mosiacism



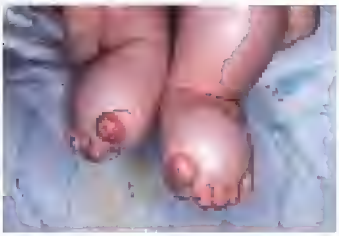
Turner Syndrome

Etiology

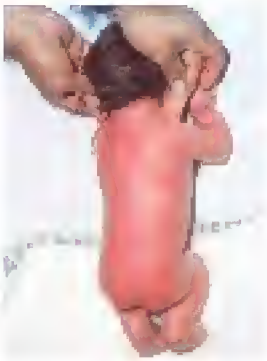
1- Classic form (45, X0) ⇒ Monosomy X-chromosome
2- Deletion of short arm of one X-chromosome.
3- Turner mosaic: - 45 X0 / 46 X X

Clinical picture

A. At birth

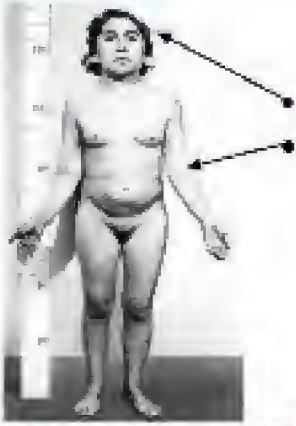


- Transient lymphoedema in dorsa of hands & feet

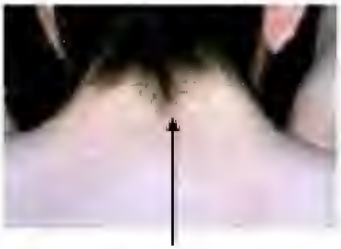


- Low birth weight
- Loose skin at neck nape

B.Later on

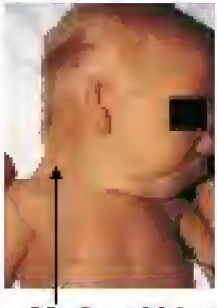


- Short female with normal mentality
- Wide carrying angle at elbow



- Low posterior hair line

- Wide spaced nipples



- Neck webbing

Diagnosis

1. For diagnosis: routine karyotyping
   Karyotyping of skin fibroblast can confirm mosaic Turner

2. For associations:
    - Echocardiography: for associated congenital heart disease: Aortic coarctation
    - Abdominal ultrasound: for ovarian dysgenesis (streak gonads) /Renal anomalies

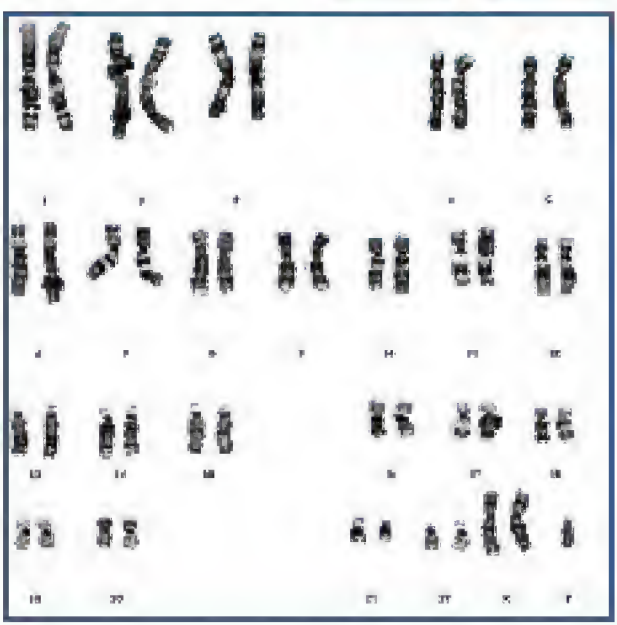
Treatment
- Growth hormone
- Estrogen replacement at 14-15 years
- Specialty consultation e.g. ENT for recurrent otitis media

Kleinfelter Syndrome

Etiology
- Extra X-chromosome in a male (47, XXY) due to non disjunction.
- May be many X -chromosomes e.g. 48, XXXY, …..

Clinical picture
- Mental retardation
- Gyneacomastia
- Diminished facial hair, feminine fat distribution.
- Atrophic testis with azospermia
- Tall stature

Diagnosis
1. Karyotyping: diagnostic (47, XXY)
2. Hormonal assay



Down Syndrome

Definition: Numerical autosomal disorder (1:700 live births) Due to Trisomy 21

The extra chromosome 21 is due to

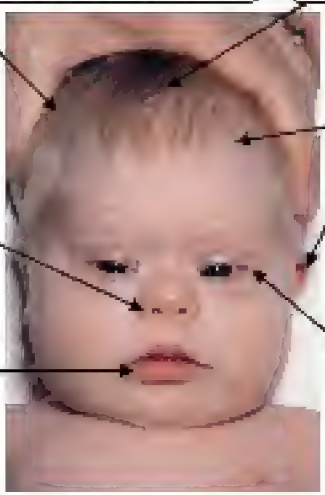
- Non disjunction occurring during gametogenesis (95% of cases)
- Translocation of an extra long arm of chromosome 21 (4% of cases)
- Mosiacism due to non disjunction occurring post fertilization (1% of cases)

Clinical picture

1. **Delayed mental milestones** → Mental retardation
2. **Delayed motor milestones:** hypotonia → hyperflexible joints; Acrobat sign.
3. **Head:**

- Mild microcephaly
- Brachycephaly (short anteroposteriorly)

- Wide posterior fontanel (at birth)
- Large anterior fontanels

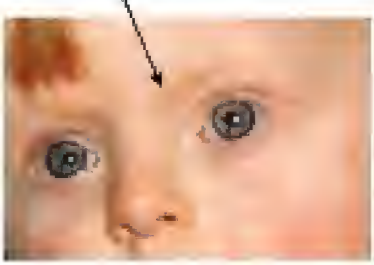


- Fine silky hair
- Low set ears

- Small nose with depressed bridge

- Small mouth
- Protruding, fissured (scrotal) tongue in a child > 6 yrs
- Delayed teething

- Hypertelorism
- Epicanthal fold
- Upward slant of eyes
- Bruchfield spots (speckled iris)

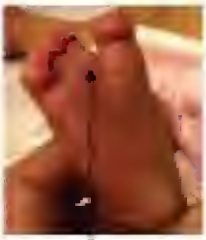


4. **Heart**
   - Congenital heart disease in about 50% of cases
   - Endocardial cushion defect and VSD
5. **Abdomen**
   - Distended with umbilical hernia
   - Visceroptosis
6. **Genitalia**
   - Small sized (hypogonadism)
   - Undescended testis is frequent

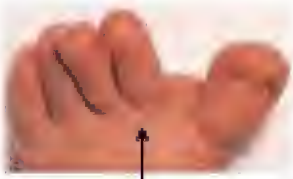
7. Hands

- Short & broad hands
- Simian crease : one transverse crease
- Clinodactyly : incurved little finger due to rudiment middle phalanx

8. Feet



- Short & broad feet



- Leading crease (Ape crease).
- Wide gap between the first and second toes

Co morbidities/complications

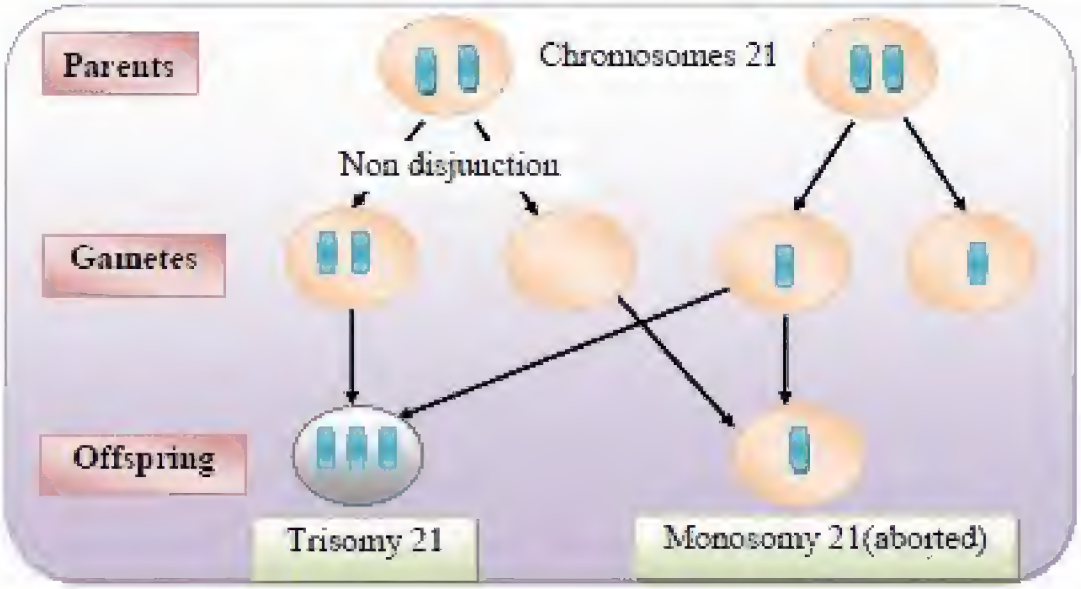
1. Immunodeficiency → recurrent infections → chest, serous otitis media
2. Neurological: - Mental retardation→ accidental trauma
   - Atlanto axial instability with risk of spinal cord injury
   - Autism spectrum disorders, early Alzheimer
   - Strabismus, cataracts, nystagmus
3. Cardiac: Congenital heart disease → recurrent heart failure& chest infection
4. Respiratory: - Recurrent chest infections
   - Obstructive sleep apnea.
5. Renal anomalies.
6. Hematological: Acute leukemia (*20 times more common*).
7. Auto immune endocrinopathies
   - Hypothyroidism
   - Diabetes mellitus
   - Addison disease
8. Gastrointestinal
   - Anomalies
     - Doudenal atresia
     - Hirschsprung disease.
     - Imporforate anus
   - Celiac disease

Chromosomal Makeup of Down syndrome

Non disjunction (Regular mongle)

Mechanism

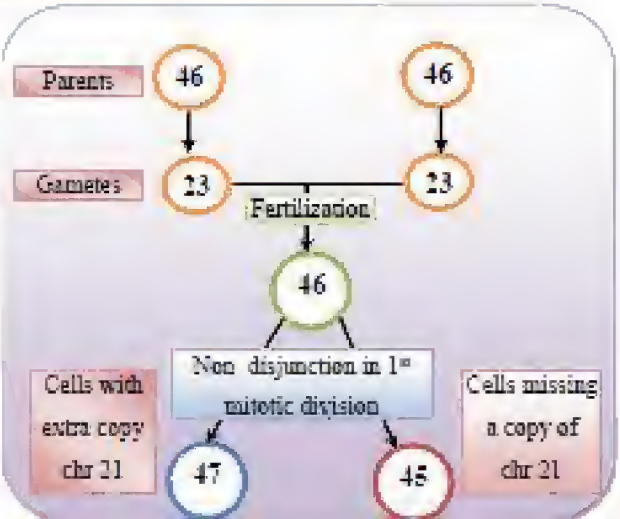
- Failure of the two chromosomes 21 to disjoin normally as it should be during gametogenesis (meiosis)→Production of gamete with an extra chromosome 21
- This extra chromosome is maternal in 97% of cases
- Recurrence rate increases with increasing maternal age (1/100 if age > 35 years)
- Baby karyotype :47 XX (+ 21) or 47 XY (+ 21); no role for parental karyotyping



Mosiac Down syndrome

Mechanism

- Non disjunction occurring post fertilization ⇩
- If occurred in the 1st mitotic division→ 2 cell lines: 47, (+ 21) + 45, (- 21)
- If occurred in the 2nd mitotic division→ 3 cell lines: 47, (+ 21) + 45,(- 21) + 46
- The patient may not show all features of mongolism



Translocation Down syndrome

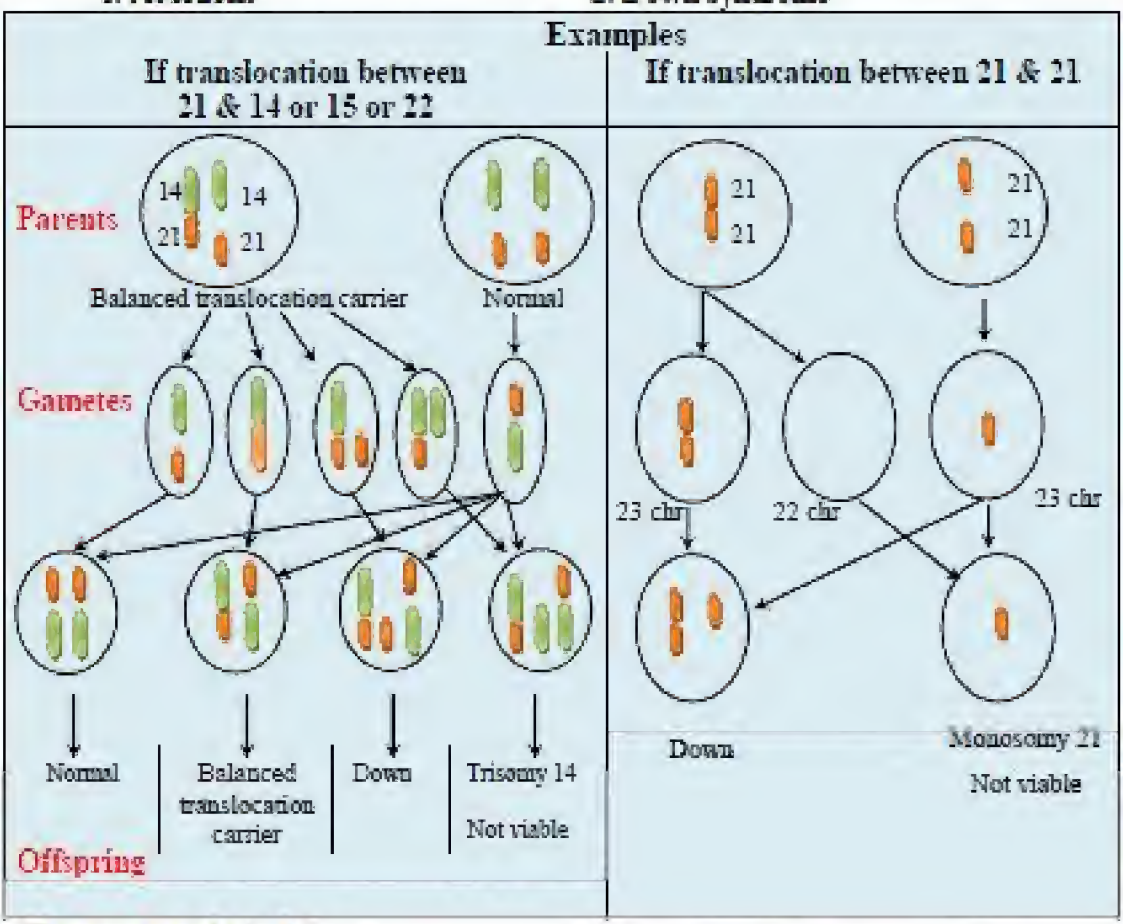
Mechanism

* Chromosome 21 is translocated onto another *acrocentric* (14, 15, 21, 22)
* The short arms of the acrocentric chromosomes contain no essential genetic material & being very short, they are easily lost→ The long arms of two acrocentric chromosomes may fuse together making one long chromosome without genetic loss.
* If translocation occur in a parent cells → he's a balanced translocation carrier.

Recurrence rate

- Outcomes of translocation between chromosome 21 & 14, 15, or 22:
  1. Abortions
  2. Balanced translocation carrier
  3. Down syndrome
  4. Normal
- Outcomes of translocation between chromosomes 21 & 21
  1. Abortions
  2. Down syndrome

Examples



Chromosomal study

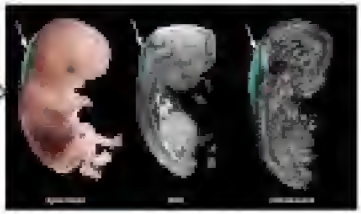
* For baby → e.g. 46, XX, (t 21q / 14q) or 46, XY, (t 21q / 14q).
* For parents → may show balanced translocation carrier.
  e.g. Balanced translocation carrier mother : 45 ,XX ,(t 21q / 14q)

Investigations

A- Prenatal diagnosis

1- Integrated Screening can detect up to 95% Down syndrome pregnancies using:

- Maternal age
- ↑ Fetal nuchal translucency (NT) thickness ⇨
- ↓Pregnancy Associated Plasma Protein A
- *Quad screen* : Maternal blood shows
  - ↓ α feto protein
  - ↓ Unconjugated estriol
  - ↑ Free β human chorionic gonadotropin (β-hCG)
  - ↑ Inhibin (Nelson text book)



2- Karyotyping for maternal amniotic fluid cells or chorionic villous sample

B. Postnatal diagnosis

1. **Clinical**: None of the clinical features is specific to Down syndrome but the associations of multiple features is usually diagnostic
2. **Karyotyping**
   a. For the baby to:
      - Confirm Down syndrome
      - Decide the type of Down syndrome and then the risk of recurrence

   b. For the parents if the baby translocation type

Health supervision of Down syndrome

- Multidisciplinary care approach is the mainstay for managment
- Screen for and manage complications

Condition	Time to screen
• Congenital heart disease	– At birth and young adult for acquired valve disease
• Strabismus, cataracts, nystagmus	– Birth or by 6 mo; by pediatric ophthalmologist – Check vision annually
• Hearing impairment or loss	– Birth or by 3 mo with auditory brainstem response or otoacoustic emission testing – Check hearing q6mo -1 year
• Celiac disease	– At 2 years or with symptoms(IgA and tissue transglutaminase antibodies)
• Hypothyroidism	– Birth; repeat at 6-12 mo and annually
• Obstructive sleep apnea	– Start at ~1 yr and at each visit – Monitor for snoring, restless sleep
• Atlantoaxial subluxation or instability (incidence 10-30%)	– Radiographs at 3-5 years or when planning to participate in contact sports, diving, swimming – Radiographs indicated wherever neurologic symptoms are present even if transient (neck pain, torticollis, gait disturbances, weakness)

Other Trisomies

	Trisomy 18 (Edward's Syndrome)	Trisomy 13 (Patau syndrome)
Incidence	1/7000 live births	1/10.000
Karyotyping	47, +18	47, +13

Clinical picture

a. Common features:

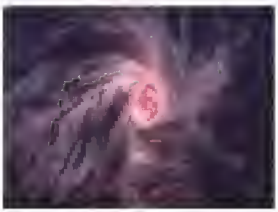
- Growth retardation
- Microcephaly and Mental retardation
- Dysmorphic face
- Congenital heart diseases (VSD, PDA , ASD)
- Visceral anomalies
- Most die in the 1st year of life

b. Specific features:

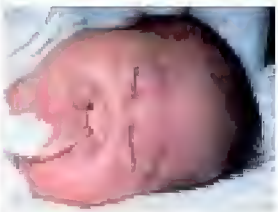
* Prominent occiput.

* Hypertonia with Closed fist and overlapping fingers

* Rocker bottom heel



* Scalp defects(cutis aplasia)
* Brain malformations



* Cleft lip and palate

* Polydactyly

Self-Assessment Case Scenarios

Case 1

15 years old girl presented to outpatient clinic for routine check ;she have not got menses yet, her height was 125 cm(< 3 rd percentile), no physical signs of puberty, with unusual facial appearance unlike her parents and her siblings; cardiac auscultation showed ejection systolic murmur over left sternal border. She is doing well in school and thyroid profile is normal.

a. Suggest a diagnosis?
b. How can you confirm diagnosis?

Case 2

A two day old male infant is referred from a community hospital for bilious vomiting and a heart murmur. The baby was born at 37 weeks gestation to a 39 year old woman who had no prenatal care. Exam: vital signs Temp 37.1 (ax), Pulse 150, Respiratory rate 45, BP 75/50, oxygen saturation 99% in room air. Height, weight and head circumference are at the 50th percentile. He appears jaundiced, and has a flat facial profile; short, upslanting palpebral fissures; a flat nasal bridge with epicanthal folds; a small mouth with protruding tongue; and single palmar creases. His lungs are clear to auscultation. His heart is tachycardic with a loud holosystolic murmur. His abdomen is non-distended. Generalized hypotonia is present. An abdominal radiograph shows a "double-bubble sign".

a. What is the most likely clinical syndrome?
b. What are the current co morbidities?
c. What are immediate lines of treatment?
d. Other workup?

Case 3

A 7-year-old patient who has Down syndrome is brought to the clinic by her mother, who is worried that the child has an increasingly abnormal gait and worsening clumsiness. On physical examination today, you note that she has an unsteady gait, and she has brisk deep tendon reflexes diffusely. These findings represent a significant change from 9 months ago when your neurologic examination showed only slightly diminished tone.

What the most likely cause of these symptoms and signs?

Case 4

A 7-year-old patient who has Down syndrome is brought to the clinic by her mother, who is worried that the child has an increasing pallor ,lethargy and abdominal distension. Examination revealed few purpuric spots, bilateral axillary and cervical lymph nodes enlargement and significant hepatosplenomegaly

What is the likely diagnosis? Two investigations required?

Diarrheal Disorders

Definition of diarrhea

* WHO defines diarrhea as: the increase of volume, fluidity, or frequency of motions relative to the usual pattern of the individual

Classification of diarrhea

i. Acute Diarrhea : - Starts acutely
- Watery without visible blood
- Last less than 14 days.

(Dysentery is acute diarrhea with visible blood in stool)

ii. Persistent diarrhea: Started as acute diarrhea (watery or dysentery) but persists more than 14 days

iii. Chronic diarrhea: - Diarrhea of gradual onset, lasting ≥ 1month or recurrent due to non infectious cause

Mechanisms of Diarrhea

A. Enteric infection

1. Type I: Non-inflammatory

- Due to
  - a. Superficial mucosal invasion due to:
    - Viral e.g. Rota virus
    - Bacterial e.g. Enteroinvasive E. coli, Campylobacter
  - b. Mucosal adhesion by e.g. Enteropathogenic E. coli ,Giardia lambelia

    Mechanism

    Superficial invasion or adherence of the absorptive villi cells with intact secretory crypt cells → crypt cells continue secretions with impaired villi cells absorption

  - c. Entero toxin production

    Example: Enterotoxigenic E coli, and vibrio Cholera

    Mechanism

    Enterotoxin stimulates adenyle cyclase enzyme in crypt cells → excessive cyclic AMP production→ excessive intestinal secretions
- Location of enteric infection: Proximal small bowel
- Illness : Watery diarrhea (*Secretory diarrhea*)
- Stool exam : No fecal leukocytes

2. Type II: Inflammatory

- Due to: Mucosal invasion and cytotoxin production
- Illness :Dysentery
- Location: Colon
- Stool exam : Fecal neutrophils and ↑↑ Lactoferin

3. **Type III: Penetrating**
   - Due to: Penetration by Salmonella typhi and para typhi, Yersinia enterocolitica
   - Illness : Enteric fever
   - Location: Distal small bowel
   - Stool exam : Fecal mononuclear leukocytes

(Nelson text book of pediatrics, 2016)

B. Osmotic diarrhea

Intestinal villi damage leads to loss of disaccharidases (e.g. lactase) → accumulation of non-absorbable solutes in intestinal lumen → osmotic load → shift of water to the intestinal lumen→ diarrhea

Differences between secretory and osmotic diarrhea

	Secretory diarrhea	Osmotic diarrhea
Volume	Large	Small
Effect of fasting	Diarrhea continues	Diarrhea stop
Food type	Unrelated	Usually related.
Stool analysis		
- Stool pH	Alkaline	Acidic
- Reducing substance	Absent	May be present
- Fecal sodium& chloride	High	Low

Acute non infectious diarrhea

1. **Dietitic**
   - Over feeding
   - Under feeding: Starvation diarrhea (scanty, greenish, ↑mucus)
   - Bad feeding: - Change in formula type or concentration
     - Introduction of new unsuitable food.
   - Lienteric diarrhea: Hyperactive gastro-colic reflex → motion short after every feed

2. **Drugs**
   - Prolonged oral antibiotics (e.g. ampicillin)
   - Laxatives to the baby or to lactating mother.

3. **Parentral diarrhea** (2ry gastro enteritis).
   - Due to infections outside GIT e.g. otitis media, respiratory infections.
   - Possible mechanisms; toxic absorption or reflex gastro intestinal irritation
   - The term parenteral diarrhea is no longer used due to possible intestinal infection.

Acute infectious diarrhea (Gastro Enteritis)

Gastroenteritis is due to infection acquired through the fecal-oral route or by ingestion of contaminated food or water

Severity

* Mild = 4-6 motions /day
* Moderate = 6-10 motions /day
* Severe > 10 motions /day

Causes of Gastroenteritis

1. **Viral** (60%)

Examples

- Rota virus.
- Norwalk like viruses
- Adenovirus

Clinical features

- Age usually less than 2 years.
- Common in winter
- May be associated upper respiratory tract infections
- Pyrexia if present usually (< 38.5 °C).
- Diarrhea is:
  - Mild to moderate.
  - Transient = (5-7 days)
  - Watery
  - Odorless

2. **Bacterial**

Clinical features

- Common in summer
- With high fever (>38.5 °C)
- Cramping abdominal pain
- Usually severe diarrhea which may be:-

* Bloody with:
  - Salmonella
  - Shigella desentyrie type 1.
  - Entero invasive E-Coli.
  - Entero hemorrhagic (*Shiga toxin producing*) E-Coli
* Watery
  - Shigella (diarrheal type)
  - Entero pathogenic E-Coli
  - Entero toxigenic E-Coli
  - Vibrio cholerae O1.
* Watery offensive for 2-4 days then turn bloody → Campylobacter jejuni.

3. Protozoal

- **Giardia Lambelia**
  - Watery
  - Offensive
  - No fever
- **Entameaba histolytica**
  - Bloody, may be with tenesmus
  - No fever usually

Complications of Gastroenteritis

1. Dehydration

- Fluid loss due to vomiting, diarrhea and anorexia (see later)
- The main cause of death in gastroenteritis

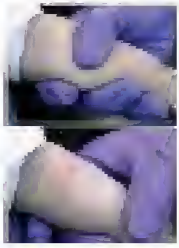
2. Shock

Types

- Hypovolemic shock with severe dehydration
- Gram negative septic shock

Clinically

- Decreased peripheral perfusion
  - Skin mottling , capillary refill time >2 seconds→
  - Cold extremities
- Decreased vital organs perfusion
  - Brain → lethargy
  - Kidney → oliguria
- Hypotension and rapid thready pulse



3. Acute renal failure (ARF)

Due to

- Hypovolemia → ↓ renal blood flow (pre renal failure).
- Untreated pre renal failure → tubular necrosis → intrinsic renal failure

Clinically

- Oliguria or anuria
- Acidotic breathing (Rapid, deep breathing).

4. Metabolic Acidosis

Due to

- Loss of bicarbonate in the stool
- Acute renal failure

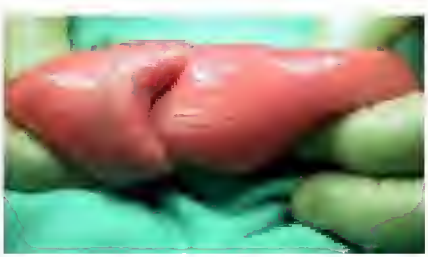
Clinically

- Acidotic breathing (rapid deep breathing pattern)
- Disturbed consciousness.
- Arterial blood gases (↓pH, ↓$PaCO_2$, ↓HCO_3)

5. **Electrolyte disturbance**
   - Hypokalemia: (serum potassium < 3 meq /L)
     Clinically - Apathy (disturbed consciousness)
     - Arrhythmias
     - Abdominal distension (paralytic ileus)
     - Atony (Hypotonia).
   - Hypocalcemia: → Tetany or Convulsions
   - Hypo or hyper natremia: → Convulsions

6. **Convulsions** → possible causes:
   - Hypoglycemia ; mainly in mal nourished.
   - Hypo or Hypernatremia.
   - Hypocalcemia
   - CNS infections e.g. meningitis or encephalitis may due to shigella or neurotropic virus

7. **Bleeding**

Possible causes	Clinically
DIC due to shock, sepsis or acidosis	- Bleeding tendency ;initially from puncture - Skin gangrene
Intussusception Part of the intestine invaginates in the distal part 	- Attacks of abdominal pain (screaming) - Vomiting with constipation - *Redcurrant* jelly stool - Sausage shaped abdominal mass - P/R → head of intussuceptum may be felt - Ultrasonography is diagnostic & safe - Air contrast enema → can be therapeutic 
Renal vein thrombosis due to severe dehydration → hypovolemia → venous stasis	- Hematuria - Flank (Renal) mass - If bilateral → acute renal failure

8. **Persistant diarrhea and eventual Malnutration**

Workup of Gastroenteritis

1. **For the cause**
   - Stool analysis for blood, fecal leucocytes , Rotazyme test,parasites
   - Stool culture
2. **For the complications** (more important)
   - Routine: Blood urea nitrogen, creatinine, sodium ,potassium, and calcium
   - Blood gases → for metabolic acidosis.
   - Coagulation profile → PT, PTT, FDPs, platelets for bleeding
   - Others: According to clinical suspicion e.g. Abdominal ultrasound /X ray

Treatment of Gastroenteritis

- **GE with no or minimal dehydration (plan A):Home management**

1. **Fluid therapy**

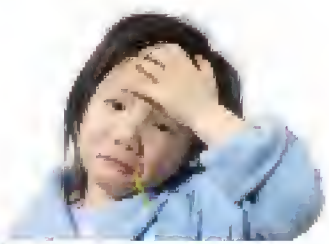
Avoid dehydration by plenty of fluid:

- Use oral rehydration solution (ORS).
- Amount of ORS:

Weight	ORS amount after each loose motion or vomiting episode
< 10 kg	60-120 ml
> 10 kg	120-240 ml

- Food based fluids for infants > 6months or weaned:
  - Rice water, soup, and yogurt drinks
  - Avoid hyperosmolar fluids as it increases the diarrhea

2. **Feeding to avoid malnutrition**
   - Continue breast feeding or usual milk formula
   - For infants > 6months, give: mashed potatoes, cereals, and BART (Banana, Apple juice, Rice, Toast)
3. **Follow up and medical advice if**
   - No improvement for 3-5 days
   - Presence of a warning sign: *(Reminder: Bloody FEVER)*
     - **Bloody** motions.
     - High **F**ever.
     - Eager to drink (Marked thirst)
     - Frequent Vomiting.
     - Excessive watery motions
     - Refusal of oral fluids or feeding.



- **GE with dehydration (plan B & C)** ⇒ *See dehydration*

- **Antibiotics**
  * Indications : - If bacterial cause is identified or strongly suspected.
    - Associated bacterial infection (e.g. otitis media)
    (Fever per se is not an indication for antimicrobial therapy)
- **Anti-parasitic**
  * Entameoba histolytica : Metronidazole 50 mg/kg /day for 10 days oral.
  * Giardia lambelia : Metronidazole 15 mg/kg for 7 days.
- **Treatment of complications e.g.**
  - Acute renal failure → Usually pre renal responds to rehydration / consult pediatric nephrologist in unresponsive cases
  - Hypocalcemia → Calcium gluconate 10% slow i.v.
  - Hypokalemia → Add potassium to the IV fluids
  - Convulsions: - Anticonvulsants (e.g. Diazepam) and treat the cause.
- **Additional therapy:**
  - Probiotics : non pathogenic bacteria e.g. *lactobacillus* .
  - Oral Zinc 10 - 20mg /day
- **Prevention of gastroenteritis**
  - Promote exclusive breast feeding for the first 6 months and continued during illness including diarrhea
  - Proper weaning
  - Rota virus (Rotarix)vaccines
  - Hygienic measures

Dysentery

Acute diarrhea with visible blood in the stool

Causes

1- Shigella Desentyrie (commonest cause).
2- Enteroinvasive E.coli and Entero hemorrhagic E- coli (O157:H7)
3- Campylobacter jejuni.
4- Salmonella (rare).
5-Entamoeba histolytica (uncommon before 5 years old)

Clinical picture

1- Acute bloody diarrhea with mucus & pus
2- Severe crampy abdominal pain
3- Tenesmus (painful defecation)
4- Pyrexia / dehydration/ toxic manifestations

Complications

1. As for acute diarrhea
2. Hemolytic uremic syndrome ; associated with *Shiga toxin* (or *Verotoxin* producing entero hemorrhagic E- coli and Shigella

Differential diagnosis

1. Intestinal obstruction e.g. Inussuception and volvolus
2. Ulcerative colitis

Investigations

- Stool analysis
- Stool culture
- CBC and blood urea and electrolytes

Treatment

* Supportive : As for acute diarrhea ; Fluid therapy , Feeding , Follow up
* Treat complications
* Treat the cause

Persistent Diarrhea (post gastro enteritis syndrome)

Definition

- Acute diarrhea (watery or dysentery) which persists more than 14 days
- About 10% of acute diarrhea progress to persistent diarrhea
- Persistent diarrhea carries high risk of malnutrition and high mortality

Etiology

1. Persistent infection e.g. Giardia lamblia, salmonella
2. Post-enteritis malabsorption:

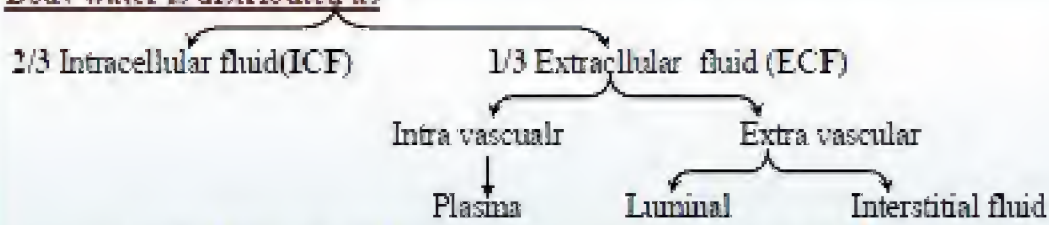
Damaged villi cells with 2^{ry} dissacharidase deficiency:

- Lactase deficiency→ Lactose intolerance (diarrhea which increases with lactose containing milks)
- Invertase deficiency →Sucrose intolerance (diarrhea which increases with sucrose containing milks)

Dehydration

Introduction

Body water is distributed as



Intracellular electrolytes		Extracellular electrolytes in meq/l	
Main cation	Main anions	Cations	Anions
Potassium (K)	Phosphate Proteinate	Na 135-145 K 3.5-5 Ca 9-11 (mg/dl) Mg 1.5 – 2.5	CL 105 HCO_3 26

Q *Infants are more susceptible to dehydration than adults, why?*

- Higher total body water; 75% of body weight in contrast to 60 % in adults .
- Higher daily requirements of water in (150 ml /kg/d)
- Higher frequency of diarrheal diseases

Definition

Dehydration means loss of water & electrolytes from ECF ; The ICF may be secondarily affected.

Etiology

1. Diarrheal diseases
2. Others : - Decreased intake e.g. starvation, coma , poor hydration in illnesses
   - Vomiting e.g. Congenital pyloric stenosis, intestinal obstruction.
   - Hyperventilation.
   - Burn
   - Fevers and hyperprexia
   - Excessive sweating
   - Polyuria e.g. diabetes mellitus, diabetes insipidus, chronic renal failure, hypercalcemia , diuretics overuse

Degrees of dehydration

1. According to degree of body weight loss (Relative to pre illness weight)

Dehydration	Body weight loss	Clinically
Minimal or absent	< 3%	Few or absent signs of dehydration
Mild to Moderate	4-9%	Typical picture of dehydration
Severe	≥ 10%	Hypovolemic shock

2. According to WHO guidelines

	Plan A	Plan B	Plan C
Definition	**No dehydration**	**Mild to moderate dehydration.**	**Severe dehydration**
General appearance	Normal, alert No shock	*Irritable, restless* No shock	*Shocked*→hypotension, ↑ pulse → lethargy, oliguria → cold mottled skin.
Eyes → look → tears	Normal Present	Slightly sunken Decreased	Deeply sunken. Absent
Mouth→ tongue → thirst	Moist Absent	Dry *Drinks eagerly*	Very dry (parched) *Unable to drink.*
Skin pinch (Turgor)	Normal Instant recoil	*Goes back slowly* Recoil in <2 sec	*Goes back very slowly* Recoil in >2 sec
Fontanel	Normal	Depressed	Depressed

N.B : - *Key signs of dehydration include: general appearance, thirst, & poor skin pinch.*
- 2 or more signs including at least 1 key sign should exist to assign certain plan

Types of dehydration

Hypotonic(Hyponatremic).	**Isotonic**(Isonatremic)	**Hypertonic**(Hypernatremic)
Serum Na < 130 meq/ L	**130 - 150 meq/ L**	**> 150 meq/ L**
A/E: Excessive intake of water or hypotonic fluids during diarrhea → loss of electrolytes > loss of water → Overhydrated cells → Marked collapse of ECF	Equal loss of water and electrolytes leading to:- → Normal cellular hydration → Collapsed ECF	Excessive intake of hypertonic fluids during diarrhea → poor absorption →↑ osmosis → loss of water > electrolytes loss → Dehydrated cells → Normal ECF
Clinical features		
Manifestations of ICF affection		
Tongue: - Moist Brain: - Lethargy - Coma - Convulsions	- Dry; thirsty - Irritable	- Very dry (woody); marked thirst - Irritable - Hyper-reflexia - Convulsions
Manifestations of ECF affection		
Shock - Rapidly occurring	- Slowly occurring	- Usually absent
Skin turgor - Marked loss	- Moderate loss	- Normal (or doughy)
Fontanels - Markedly depressed	- Moderately depressed	- Normal or bulging
Eyes - Markedly sunken	- Moderately	- Mildly sunken

Complications of dehydration

Complications of gastro enteritis plus

- Hemoconcentration → phlebothrombosis especially in cortical & renal veins.
- Hypokalemia → aggravated by rapid correction of acidosis → intracellular shift of potassium
- Hyperkalemia :
  - Aggravated by: Acidosis and excessive potassium infusion in presence of renal impairment.
  - Manifested by: - Restlessness
    - Cardiac arrhythmias (bradycardia, cardiac arrest)

(N.B: Potassium disorders are readily detectable by ECG)

- Hypernatremic dehydration hazards:

1. Seizures may be due to:
   * Intracranial hemorrhage: Brain cells dehydration →↓ brain volume → tear of intracerebral & bridging blood vessels.
   * Rapid lowering of serum Na → brain cells overhydration → brain edema.
   * Associated Hypocalcemia is common.
2. Renal tubular injury → acute renal failure

Treatment of dehydration

I. Mild to moderate dehydration (Plan B dehydration)

❶ Deficit therapy

- Fluid type ? → Oral rehydration solution (ORS)
- Amount ? → 50-100 ml/kg over 4 hours (if child wants more, give more)
- Route ? → One tea spoonful/1-2 minutes orally

Problems during deficit therapy

Problem	Management
• Vomiting	* Wait 10 minutes * ORS is given at slower rate (spoon / 2-3 minutes)
• Refusal of ORS • Frequent vomiting	* ORS can be given more slow by nasogastric tube
• Coma • Persistent vomiting • Abdominal distension • Paralytic ileus. • Rapid loss of stool	* Deficit therapy is given parenterally (IV) • Amount of fluid: 50-100 ml/kg • Type of fluid: – Poly electrolyte solution (Polyvalent) or – Glucose: Saline mixtures : 5% dextrose in ½ Normal saline

❷ **Feeding**

* Breast fed → continue
* Non breast fed → give usual formula after the first 4 hours
* If child > 6 months or weaned → give plenty of fluid and food as in plan A.

❸ **Assessment after deficit**

- **Good response**
  * Criteria: - No signs of dehydration
    - Baby fall asleep
    - Pass urine
  * Decision: Continue replacement as for plan A(see before)
- **Still dehydrated** → Repeat the deficit therapy
- **Worsening** (Severe dehydration) → Treat as plan C

II . Severe dehydration (Plan C dehydration)

❶ **Shock therapy**

- Fluid type ? → lactated Ringer (or physiological saline).
- Amount ? → 20 ml/kg over ½- 1 hour
- Route ? → Parenteral(intravenous or intraosseus)

After shock therapy

- **Good response**
  - Criteria: - Improved mental state
    - Improved perfusion
    - Able to drink
  - Decision: Treat as for mild to moderate dehydration (R/ **Deficit Therapy**)
    Give 100 ml/kg of previous fluids over 4 hours
- **Still shocked**
  - Criteria: Lethargic, weak pulse, poor capillary refill
  - Decision: - Repeat shock therapy.

❷ **Assessment**

After 6 hours in infants<1 year and after 3 hours in older child

Finding	Decision
Severe dehydration	- Restart rehydration therapy as for plan C - Think of and treat complications
Mild to moderate dehydration	- Continue as plan B
No signs of dehydration	- Continue as plan A

❸ **Feeding** ⇒ As in plan B

Don't forget: Specific treatment (e.g. Antibiotics) and treat complications

Precautions during hypernatremic dehydration treatment

- Type of fluid: Glucose 5% in ½ normal saline
- Under correction → water deficit should be replaced over more than 36 hours
- Slow correction → Reduce serum Na by no more than 0.5 mEq/L per hour
- Monitor serum Na & Ca closely during treatment.
- If convulsions occur during treatment → treat the cause:
  - * Rapid lowering of Na → NaCl 3% 2-4 ml/kg very slow i.v
  - * Hypocalcemia → Ca gluconate 10% 1-2 ml/kg very slow i.v
  - * Brain edema (due to rapid or over hydration) → mannitol 20% over 20min.

(See Prevention and treatment of viral gastroenteritis in children, UpToDate)

Oral rehydration solution (ORS)

* **Mechanism of ORS** → co absorption of Na & glucose or certain amino acids even via damaged intestinal mucosa → other electrolytes esp. Chloride are absorbed 2ry to Na.

1. Standard ORS(Rehydran sachets)
   - Rehydran sachets: each sachet contain:-

- Sodium chloride	0.7	Gram
- Sodium citrate	0.5	Gram
- Potassium chloride	0.3	Gram
- Glucose	4	Gram

   Each sachet is dissolved in **200 ml** clean water
   - WHO ORS → Contains same ratios as Rehydran ; dissolved in **1** liter
2. Other types of ORS:
   - Lohydran → With lower sodium chloride content
   - ReSoMal: - ORS containing less Na , more K with added magnesium & zinc.
     - Mainly for rehydration of severely malnourished infants.

Advantage of ORS	Limitations of ORS
Fit for	**Not fit for**
• All types of dehydration	• Shocked cases (unable to drink)
• Any age even the newborn	• If intra venous fluids are indicated
• Any type of diarrhea	• Glucose malabsorption (rare)

Malabsorption Syndrome

Definition

- Diminished intestinal absorption of one or more dietary nutrients
- Due to either defective nutrient digestion or mucosal absorption
- Steatorrhea → with fat malabsorption = pale, bulky, greasy, offensive stool

Etiology

1- Impaired digestion

* Hepatic
  - Biliary atresia (bile salt insufficiency)
  - Chronic hepatitis
* Pancreatic:
  - Prolonged protein calorie malnutrition
  - Cystic fibrosis
  - Chronic pancreatitis
  - Shwachman-Diamond syndrome

2- Intestinal stasis
- Protein caloric malnutrition (acini atrophy).
- Stagnant loop syndrome.
- Inflammatory bowel diseases:
  - Crohns' disease
  - Ulcerative colitis

3- Impaired absorption

a. Generalized malabsorption:

- Chronic infections: e.g. giardia lamblia, tuberculous enteritis , bilharziasis
- Congenital: chloride diarrhea, sodium diarrhea
- Defective enterocyte differentiation: microvillous inclusion disease, congenital tufting enteropathy
- Short bowel syndrome
- Celiac disease
- Auto immune entropathy
- Allergy: Multiple food protein hypersensitivity
- Intestinal tumors

b. Specific malabsorption:

Type	Example
Specific carbohydrate malabsorption	- Lactose malabsorption - Glucose galactose malabsorption - Fructose intolerance
Specific fat malabsorption	- Abetalipoproteinemia
Specific amino acids malabsorption	- Enterokinase enzyme deficiency - Hartnup disease(neutral amino acids) - Blue diaper syndrome(tryptophan)

Type	Example
Specific vitamin malabsorption	- Vitamin D , folic acid , B_{12}
Specific mineral malabsorption	- Acrodermatitis enteropathica(zinc) - Menkes disease (copper)

Clinical picture

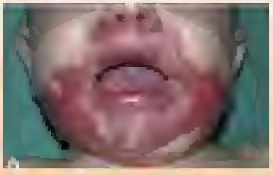
1- Features suggesting a cause e.g.- Hepatomegaly & jaundice in chronic liver disease.
- Relation to certain food in celiac disease.

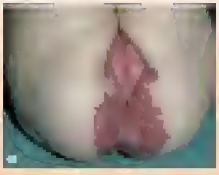
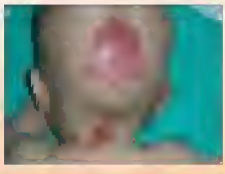
2- General ill health with pallor, weakness & failure to thrive

3- Gastrointestinal manifestations of malabsorption
- Mouth ulcers & glossitis
- Abdominal distension & flatulence
- Steatorrhea : pale, bulky, greasy, offensive stool
- Chronic diarrhea

4- Nutritional deficiency manifestations
- Fat : Loss of subcutaneous fat
- Proteins: Nutritional edema , muscle wasting & loss of weight
- Carbohydrates : Hypoglycemia
- Minerals and vitamin deficiency

N.B: **Acrodermatitis enteropathica** (autosomal recessive Zinc malabsorption):
- Dermatitis → peri facial and peri anal & extrimities
- Alopecia.
- Chronic diarrhea→ protein losing enteropathy



Investigations

A- Stool examination to prove malabsorption

* For carbohydrate malabsorption:
  - Stool pH (may be acidic)
  - Reducing substances in stool.
  - Breath hydrogen test.
* For fat malabsorption:
  - ↑ Stool fat globules.
  - ↑ Stool fat content (Steatocrit test).
* For protein malabsorption.
  - ↑ Fecal α_1 antitrypsin.

B- For the cause:

STEP 1

- Intestinal Microbiology
  - Stool cultures
  - Microscopy for parasites
  - Viruses
  - Breath hydrogen test
- Screening Test for Celiac Disease
- Sweat chloride test for cystic fibrosis.
- Noninvasive Tests for:
  - Intestinal function e.g. iron absorption test
  - Pancreatic function (amylase, lipase, fecal elastase)
  - Intestinal inflammation (fecal calprotectin, rectal nitric oxide)
- Tests for Food Allergy: Prick/patch tests for foods
- Abdominal Ultrasounds (Scan of Last Ileal Loop)

STEP 2

- Evaluation of Intestinal Morphology:
  - Endoscopy and jejunal/colonic histology /Electron microscopy
  - Imaging (upper or lower bowel series, capsule endoscopy and the new SmartPill measures pressure, pH, and temperature)

STEP 3: Special Investigations:

- Intestinal immunohistochemistry
- Anti-enterocyte antibodies
- Serum catecholamines
- Autoantibodies
- Brush-border enzymatic activities
- Motility and electrophysiologic studies

(Nelson textbook of pediatrics, 2016)

Treatment

1- Treat the cause (medical or surgical)

2- Adequate nutrition → Avoid causative food
→ Medium chain triglycerides
→ Supplemental minerals & vitamins.

Celiac disease

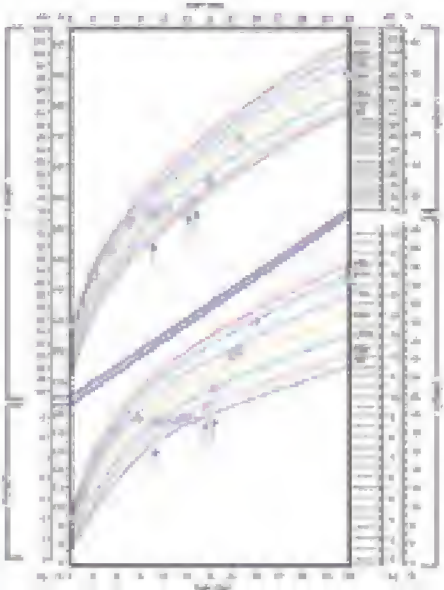
Definition

- An immune-mediated (T-cell) systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals
- Triggered by the ingestion of wheat gluten (contains epitopes from gliadin which are highly resistant to intraluminal and mucosal digestion) and related prolamines from rye and barley → incomplete degradation favor the immunostimulatory and toxic effects → severe intestinal mucosal damage (**Gluten Sensitive Entropathy**).
- Frequent associations
  - Type 1 diabetes, autoimmune thyroid disease, Addison disease, selective IgA deficiency, intestinal lymphoma and rheumatoid arthritis
  - Down, Turner, and Williams syndromes

Clinical spectrum

Symptomatic:

1. Frank malabsorption
   - Chronic diarrhea (steatorrhea) with large pale, bulky, greasy, offensive stool
   - Present around 6^{th} – 12^{th} month with feeding gluten diets
   - Abdominal distension & pain → irritability
   - Features of malabsorption syndrome (*see before*)
   - Failure to thrive due to steatorrhea & marked anorexia
   - Finger clubbing
2. Extra intestinal manifestations:
   - Iron-deficiency anemia, unresponsive to iron therapy (most common)
   - Short stature
   - Arthritis and arthralgia
   - Aphthous stomatitis
   - Peripheral neuropathies
   - Cardiomyopathy
   - Isolated hypertransaminasemia



Growth curve demonstrates initial normal growth from 0-9 mo, followed by onset of poor appetite with intermittent vomiting and diarrhea after initiation of gluten-containing diet *(single arrow)*. After biopsy confirmed diagnosis and treatment with gluten-free diet *(double arrow)*, growth improves

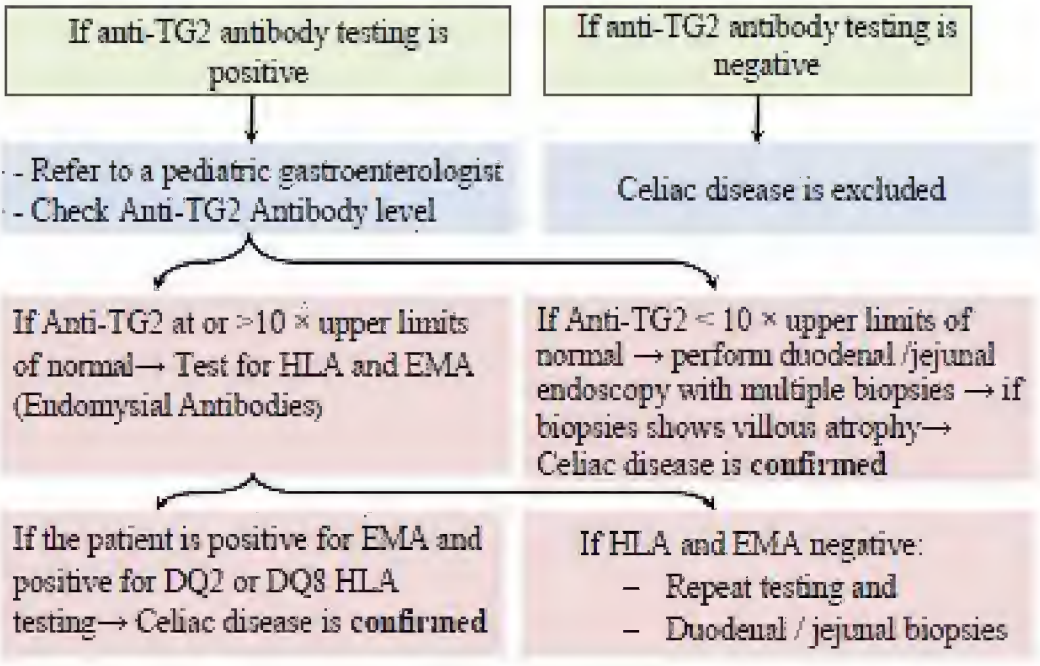
(Nelson 2016)

Silent
- No apparent symptoms in spite of histologic evidence of villous atrophy
- In most cases identified by serologic screening in at-risk groups

Potential
- Subjects with positive celiac disease serology but without evidence of altered jejunal histology

Diagnosis

1. **Symptomatic patients**
Test for IgA anti Tissue Trans Glutaminase 2 antibodies (anti-TG2 IgA antibodies) and in addition for total IgA in serum to exclude IgA deficiency



2. **In asymptomatic cases:** diagnosis of celiac is determined by biopsy
3. **Diagnosis confirmation:**
Diagnosis is confirmed by an antibody decline, and preferably, a clinical response to a gluten-free diet.
4. **If diagnostic uncertainty remains:**
Gluten challenge and repetitive biopsies

Treatment
- Lifelong strict adherence to a gluten-free diet (use maise & rice) regardless of the presence of symptoms with aid of an experienced dietician
- Monitoring for symptoms, growth, physical examination, and adherence
- Periodic measurements of TG2 antibody levels to document reduction in antibody titers

(Nelson textbook of pediatrics, 2016)

Self-Assessment Case Scenarios

Case 1

A male patient aged one-year presented to the ER room with history of severe watery diarrheal attack two days back but with minimal vomiting but since this morning vomiting becomes more intractable with loose stool with mucous and blood. On examination, he was crying with sunken eyes, severely irritable , temperature 38◦C, thready pulse and moderate dehydration.

a. **What is the diagnosis?**
b. **Investigations?**
c. **Management?**

Case 2

A 9 months old baby girl, formula fed, presented to you with vomiting and diarrhea for previous 12 hours. On examination she was found lethargic, deeply sunken eyes, skin recoil after more than 2 seconds and capillary refill time >3 seconds (normal < 2 seconds). Her current weight is 5.5 kg

a. **What is the degree of dehydration?**
b. **What should be initial line of treatment?**

Case 3

An 18 month old male is brought to the emergency department with a chief complaint of diarrhea and vomiting for 2 days. His mother describes stools as liquid and foul smelling, with no mucous, or blood. He reportedly is unable to keep anything down, vomiting after every feeding, even water. He has about 6 episodes of diarrhea and 4 episodes of vomiting per day. He has a decreased number of wet diapers. Exam: temp 37.0, Pulse 110, RR 25, BP 100/75, weight 11.3 kg (40th percentile). He is alert, in mother's arms, crying at times, and looks tired. Minimal tears, lips dry, mucous membranes tacky, His diaper is dry. No rashes are present. His capillary refill time is less than 3 seconds and his skin turgor is slightly diminished.

a. **What is the degree of dehydration**
b. **How far ORS is suitable for this baby?**
c. **What are amount of required fluids?**

(Source: Case Based Pediatrics, Hawaii University)

Infections

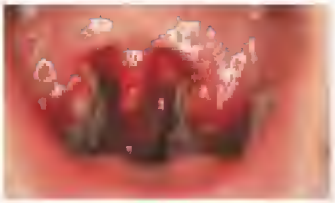
Scarlet fever

Etiology

* Group A β hemolytic Streptococci (GAS) that produce erythrogenic toxin
* Transmitted by droplet infection
* Incubation period: 3 days

Clinical picture

Throat



- Sudden onset of fever and sore throat
- Tonsils are red, enlarged with patches of exudates which may form a membrane
- Pharynx is red and edematous

Tongue

- In the 1st two days:
  White strawberry tongue (white coated tongue with red edematous papillae)
- By the 5th day:
  Red strawberry tongue (shedding of the white coat leaving red tongue with prominent papillae)

Skin rash

- Diffuse red maculopapular, fine punctate → Goose skin appearance.
- Appears on the 2nd day of the disease.
- Starts in around neck then spread to the trunk.
- Rash is more intense in deep creases (e.g. elbow) → and don't blanch on pressure (Pastia's Lines).
- In the face; it spares the peri oral area → Flushed face with circum oral pallor
- Rash fades with peeling at the fingers and toes after 3- 7 days

Investigations

- Lecucocytosis with neutrophelia
- Positive throat culture.
- Raised ASO titer >250 Todd units ;peaking in the second week

Complications

- **Early (suppurative; septic)**: in the 1st week of illness

A. Local

- Acute otitis media, mastoiditis
- Sinusitis
- Retropharyngeal abscess
- Cervical lymphadenitis

B. Distant(rare)

- Meningitis
- Bronchopneumonia
- Arthritis
- Septicemia

- **Late (non suppurative; aseptic)**: after a latent period (2-3 weeks)
  - Acute rheumatic fever
  - Acute glomerulonephritis
  - Post streptococcal reactive arthritis (non migratory, small and large joints)
  - Erythema nodosum ; red, raised, tender nodules over the chin of the tibia
  - Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus pyogenes (PANDAS) includs tics disorders, obsessive compulsive disorders and Tourette syndrome

Differential diagnosis

a. Other causes of tonsillar membrane
   - Infectious mononucleosis
   - Oral moniliasis
   - Agranulocytosis
   - Vincent's angina

b. Other causes of strawberry tongue
   - Kawasaki disease
   - Staphylococcal toxic shock syndrome
   - Streptococcal toxic shock syndrome

Treatment

1. Symptomatic: bed rest, light diet, anti pyretics and adequate fluid intake.
2. Antibiotics options
   - Oral penicillin V for 10 days
   - Once daily amoxicillin (50 mg/kg, maximum 1,000 mg) for 10 days
   - Single intramuscular injection of benzathine penicillin G
   - Erythromycin or azithromycin for penicillin sensitive patients

Pertussis (whooping cough)

Etiology

- Organism: Borditella pertussis & Borditella parapertussis
- Route of infection: Droplet infection (mainly in child < 5years)
- Incubation period: 1-2 weeks.

Clinical picture

1. Catarrhal stage

- The most infectious stage (1-2 weeks)
- Coryza
- Conjunctivitis
- Cough
- Mild fever

2. Paroxysmal stage

- Lasts for 4- 6 weeks up to 10 weeks
- Paroxysms of cough
  - Series of > 5 cough in single expiration followed by a whoop (forcible inspiration against narrow glottis).
  - During the attack; there's facial redness, bulging eyes, tongue protrusion and distended neck veins.
  - Post tussive vomiting is very common
  - After the attack; patient appears drowsy and exhausted.
  - Paroxysms may be triggered by eating, drinking , and exertion
  - Paroxysms are more worse at night

3. Convalescence stage

- Lasts for 1-2 weeks
- Gradual decline in severity of paroxysms but cough may last for months

Complications

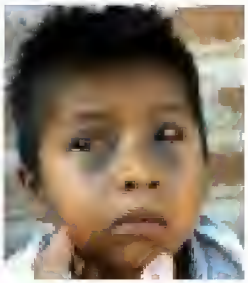
More frequent in infants and young children

1. Secondary infection

- Bronchopneumonia / pneumonia usually with staphylococci or streptococci
- Otitis media
- Activation of dormant tuberculosis infection
- Atelectasis

2. Seizures; may be due to:
   - Cerebral hypoxaemia
   - Intracranial hemorrhage.
   - Tetany (severe vomiting → alkalosis → ↓ ionized Calcium)

3. Straining in paroxysms can lead to
   - Sub-conjunctival hemorrhage
   - Epistaxis
   - Intracranial hemorrhage
   - Ulcers of tongue frenulum.
   - Pneumothorax
   - Hernias ; umbilical & inguinal.
   - Rectal prolapse.



4. Malnutrition

Due to anorexia , vomiting , and faulty food restriction

Diagnosis

In catarrhal stage

- History of contact with to a typical case
- Nasopharyngeal swab and direct fluorescent antibody staining
- Nasopharyngeal swab and PCR or Culture

In paroxysmal stage: Typical paroxysm with:

- Absent fever, wheezes or rales
- Cough ≥ 14 days
- Apnea in infants less than 3 months

Differential diagnosis: from other causes of:

a. **Spasmodic cough:**

1 Pertussis
2. Adenovirus infection; associated with sore throat and conjunctivitis.
3. Foreign body inhalation
4. Pneumonia: Interstitial or Mycoplasma
5. Mediastinal mass e.g. lymph node compressing the trachea.
6. Bronchiolitis

b. **Other causes of chronic cough** e.g.

1. Bronchial asthma: - Recurrent wheezy chest
   - Related to allergens or exercise
   - Respond to bronchodilators
   - Relatives with asthma
2. Pulmonary tuberculosis

Treatment

1. Cases

a. General

- Isolation and Bed rest
- Avoid triggers of cough(e.g. hyperactivity)
- Cough sedatives
- Care of feeding: small frequent feeds or tube feeding

b. Antibiotic

* Values
  - Reduction of infectivity period
  - Possible clinical improvement.
* Choice
  - Azithromycin 10 mg/kg/day for 5 days
  - Clarithromycin 15 mg/kg/day for 7 days
  - Erythromycin 50 mg/kg/day for 10 days

2. Prevention

- Active immunization : DTaP vaccine
- Antibiotic as for contacts regardless immunization state ± Booster dose of DTaP
- Intra muscular pertussis immunoglobulin for contacts below 2 years

Self assessment case scenarios

Case 1

An infant aged 29 days was taken by her parents to a local emergency department with difficulty breathing. The infant had been coughing for approximately 5 days with increasing severity, resulting in post tussive vomiting and several choking episodes. At presentation, the infant was lethargic, and examination revealed tachycardia and mild fever .He had thick, foamy mucus coming from his mouth, appeared cyanotic, and had an O2 saturation of 70%.Laboratory results revealed severe lymphocytosis and a chest radiograph revealed perihilar infiltrates

The infant's mother, aged 20 years, has a prolonged paroxysmal cough with post tussive vomiting and gasping for air that began approximately 3 weeks before the infant's delivery

a. **What is the diagnosis?**
b. **How to confirm diagnosis?**

Enteric Fever (typhoid fever)

Etiology

- Organism: Salmonella typhi & paratyphi (A,B,C) ⇒ G-ve bacilli
- Route of infection: faceo-oral route from cases or carriers
- Incubation period: 2 weeks

Clinical picture

1. In young infants

- Acute onset of fever , vomiting , and diarrhea
- A picture mimic bacillary dysentery and dehydration

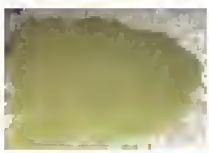
2. In older child: Like adult typhoid

Fever

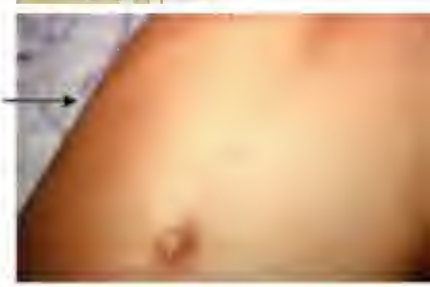
- Has a stepladder rising pattern ; plateau at 39-40 C° by the end of 1st week
- Associations
  - Headache, prostration , anorexia , chills and dry cough
  - Coated tongue
  - Relative bradycardia

Abdominal

- Diffuse abdominal pain
- Diarrhea (*Pea-soup*) may occur early but constipation predominates later



- Splenomegaly : small , soft and tender
- Rose spots :
  - Salmon-colored, blanching, truncal, maculopapules
  - Appear by the 5th day and resolve within 5 days

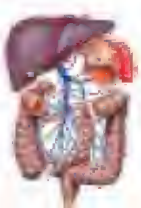


Outcome

* By the end of the 1st week the patient may appear acutely ill , lethargic with convulsions (*status typhosus*)
* Convalescence starts after 4 weeks by decline in temperature and improvement of the general condition .
* Relapse may occur within 4 weeks from decline of fever

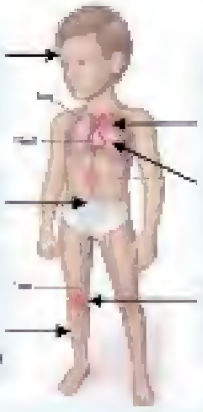
Complications

- Gastro intestinal
  - Intestinal hemorrhage and perforation by end of 2nd week
  - Cholycystitis (possible carrier state)
  - Perisplenitis



- Gastroenteritis→ dehydration and electrolyte disturbances

- **Other rare complications**



- Toxic encephalopathy
- Cerebral thrombosis
- Cystitis (possible carrier state)
- Osteomyelitis
- Septic arthritis

(In sickle cell disease and diabetes)

- Pneumonia
- Empyema
- Carditis
- Congestive heart failure
- Deep venous thrombosis
- Arteritis

Relapse; May occur within 4 weeks from drop of temperature

Diagnosis

- The mainstay of diagnosis of typhoid remains clinical in much of the developing world
- Blood culture is positive in 40-60% of cases early in the disease
- After the 1st week
  a. Widal test (Positive titer >1/160)
     - Detect antibodies against O & H antigens
     - Never used alone to prove the diagnosis in endemic areas
  b. Positive stool culture and urine culture
- Other investigations:
  a. CBC:
     - Anemia & leucopenia (toxic depression of bone marrow).
     - Thrombocytopenia is a marker of severity
  b. Nested polymerase chain reaction analysis using H1-d primers has been used to amplify specific genes of S. Typhi in the blood of patients
  c. Culture of bone marrow cells (not affected by prior use of antibiotics but invasive)

Treatment

1. Cases

a. General

- Bed rest & light diet
- Symptomatic treatment
- Treat complications:
  - Intravenous line and intravenous fluids for shock
  - Blood transfusion for hemorrhage
  - Surgical consult for intestinal hemorrhage and/ or perforation

b. Antibiotics choice

- For fully sensitive and uncomplicated enteric fever
  - Chloramphenicol or ampicillin for 14-21 days(high relapse rate) or
  - Alternative: Flouroquinolone
- For multidrug resistant (*to ampicillin, septrasole, and chloramphenicol*)
  - Flouroquinolone or
  - Cefixime or Ceftriaxone
- For quinolone resistant enteric fever
  - Azithromycin for 7 days or
  - Ceftriaxone for 10-14 days

2. Prevention

- Food & water hygiene
- Vaccine → Ty21a or Vi capsular conjugate vaccine (TAB vaccine is obsolete)

Self assessment case scenarios

Case 2

A 12-year-old child developed fever about 1week after visiting relatives in the village. The fever has persisted for about 10 days. Diarrhea was present for a few days, and then cleared. The child is now constipated. The child appears moderately acutely ill. The liver and spleen are enlarged. There are palpable, small (2–4 mm) erythematous spots on the trunk only.

What is the most likely cause of this child's infection?

Case 3

A seven-year-old girl presented to our hospital with fever, abdominal pain, nausea, vomiting and diarrhoea for one week duration, followed by fresh bleeding per rectum after 10 days from her illness . She had history of neither chronic medical disease nor surgical operation. Physical examination on admission revealed pallor, BP = 80/50 mmHg, pulse rate = 97 b/m, rapid respiration , temperature = 40.2 °C. Her abdominal examination revealed mild splenomegaly with diffuse abdominal tenderness. Blood profile showed a hemoglobulin of 7.1 g/dl, and white blood cell of 4500

An urgent colonoscopy revealed multiple variable size punched-out ileal ulcers

a. **What is the diagnosis?**
b. **What are the important four lines of management?**

(Journal of Medical Case Reports *2010, 4:171*)

Tetanus (Lock Jaw)

Etiology

Clostridia tetani (gram positive spore forming, anaerobic bacilli)

↓

Spores excreted in animal excreta → contaminate soil and water

↓

Contaminate wounds, umbilical stump, surgical & vaccine sites

↓

Spores germinate → proliferate locally → produce 2 toxins (tetanospasmin & tetanolysin) which travel along nerve trunk & blood stream

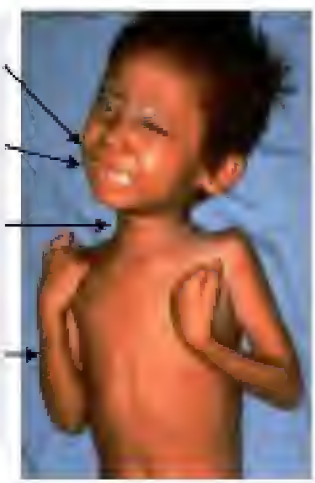
↓

Reach the CNS then redistribute to spinal cord, brain & motor end plate.

Clinical picture

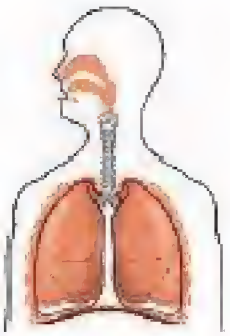
Incubation period: 1-14 days but may be longer

1. **Mild tetanus**
   * Pain & stiffness at site of injury for few weeks
   * Occur in patients who received the antitoxin before
   * Mortality < 1%
2. **Generalized tetanus** (typical form)
   * Spasms occur in descending form with intact consciousness:
   * Spasms precipitated by visual or auditory stimuli
     - Risus sardonicus : grimacing face due to facial muscles spasm
     - Trismus: difficult moth opening due to massetter spasm.
     - Laryngeal spasm → stridor and may be suffocation
     - Opisthotonus → arched back
     - Tonic seizures → flexed adducted arms and extended lower limbs with colonic



3. **Cephalic tetanus**
   - Follow head injury or otitis media.
   - Short incubation period with high mortality
   - Involve cranial nerves palsy.
   - May be followed by generalized form
4. **Tetanus neonatorum** (due to contaminated newborn's umbilical stump)

Complications



a. Respiratory
- Laryngeal spasm → suffocation
- Aspiration pneumonia
- Pneumothorax
- Lung collapse.

b. Mechanical: (with severe seizures)
- Tongue laceration
- Vertebral fractures
- Muscle heamatoma.

Diagnosis

1- History of wound and typical spasms
2- Normal CSF.
3- Wound culture may be helpful.

Treatment

I. Prevention

1. Active immunization
- DTaP or DT At 2, 4, 6, 18 months
- Booster dose at 4 years

2. Prevention of tetanus after injury:

a. Surgical management of the wound (better left opened.)

b. Prophylaxis as follows (according to immunization history):-

1. Unknown or received less than 3 doses of toxoid
* Booster dose of diphtheria toxoid vaccine
* Tetanus immunoglobulin(500units) or tetanus antitoxin(5000 units) for contaminated wounds

2. If received 3 doses or more of toxoid

Ask for the time of last toxoid dose:
* In clean wounds
  - Last toxoid dose ≥ 10 years → booster dose
  - Last toxoid dose < 10 years → nothing
* In contaminated wounds
  - Last toxoid dose ≥ 5 years → booster dose
  - Last toxoid dose < 5 years → nothing

3- Prevention of tetanus neonatorum:
- Maternal immunization with tetanus toxoid
- Aseptic care of the umbilical stump

II. Curative

1- The patient is kept in quiet, dark room.

2- Supportive → I.V fluids

→ Respiratory Care:

- Suctioning.
- Keep patent airway
- Oxygen inhalation
- May need assisted ventilation.

3- Diazepam I.V for spasms (0.1 – 0.3 mg/kg)

4- Toxin neutralization

- Tetanus immunoglobulin 3000-6000 IU
- Anti tetanic serum (tetanus antitoxin) 50.000-100.000 IU

5- Penicillin G 200.000 IU/kg/d I.V for 10 days.

6- Immunization after recovery

Self assessment case scenarios

Case 4

A seven-day-old male baby was admitted to the Intensive Care Unit with progressive difficulty in feeding, hypertonicity, and severe tonic contractions of the muscles triggered by minimal stimuli such as light, noise or touch.

The patient was afebrile and eupneic, weighing 2800 g, and had a history of nonsterile home delivery.The laboratory evaluation was within normal except for Culture from the umbilical cord grew several aerobic bacterial species

(a)

(b)

1. **What is the diagnosis?**
2. **What are the clinical signs seen?**

Case 5

A 5-year-old unimmunized child fell while playing in an old barn and sustained a laceration to his leg. **After local wound care, what would be the most appropriate management regarding tetanus prophylaxis?**

Viral Infections

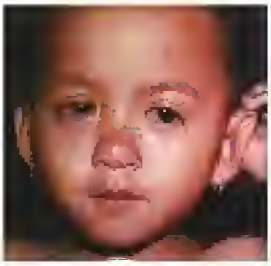
Measles (Rubeola)

Etiology

- RNA virus One antigenic type, so, one attack gives lifelong immunity
- Transmitted by droplet infection.
- Incubation period 1-2 weeks
- Infectivity period 5 days before & 5 days after rash

Clinical picture

a. **Catarrhal stage**



- High fever
- Non purulent conjunctivitis with photophobia.
- Coryza (mucopurulent rhinits)
- Cough (dry, irritating, barking)
- Sore throat

Koplick's spots (pathognomonic)

- Appear on the 3rd day of fever
- Opposite the lower molar teeth
- Grayish white dots with red areolae.
- Disappear 2 days after rash

b. **Eruptive stage**

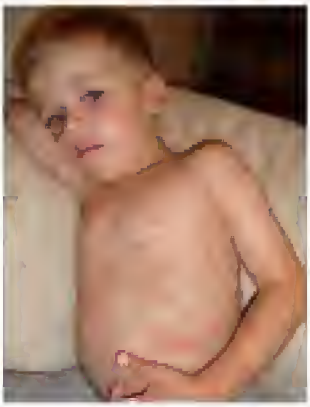
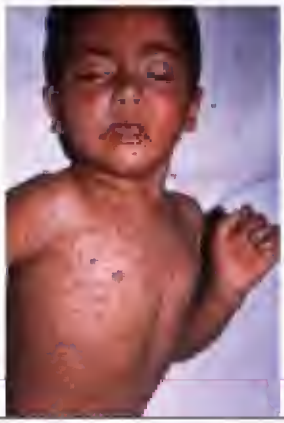
1. **Fever /rash relationship**
   - Rash usually appear on the 4th day of fever
   - Fever rises up to 40 °C for 2 days then rapidly fall
2. **Rash pattern**

   - Maculopapular rash
   - Starts behind the ears near the hair line
   - By the 1st day it covers the upper half of the body
   - By the 2nd day it covers the lower body till the thigh
   - By the 3rd day it reaches the feet When it reaches lower limbs, it fade from the face over the next 3 days

c. **Convalescence stage**

Rash fade in order of appearance with fine branny desquamation (except in palms & soles)

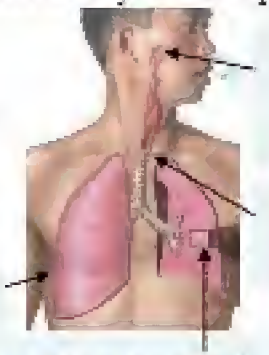
Measles variants

Modified (attenuated) measles	Atypical measles
	
Seen in patients with preexisting but incompletely protective anti-measles antibody e.g. – Receipt of intravenous immunoglobulin – Measles vaccination	Seen in patients who received killed measles vaccine (obsolete) and in immune compromised – Confluent bullous or hemorrhagic rash – Bleeding rash and orifices – Multi organ involvement

Complications

1. Pulmonary infections

- Commonly 2^{ry} bacterial infection mainly with strept pneumoniae
- with streptococci
- Suggested by:
  - Marked increase of fever decline
  - Malaise and prostration
  - Leucocytosis

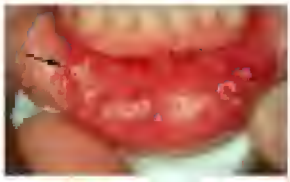


- Otitis media
- Sinusitis
- Tonsillopharyngitis
- Laryngitis
- Tracheobronchitis
- Pneumonia
- Hect's pneumonia : viral pneumonia with multinucleated giant cells in the lungs.
- Activation of T.B focus : due to temporary loss of hhypersensitivity to tuberculoprotein for 4-6 weeks

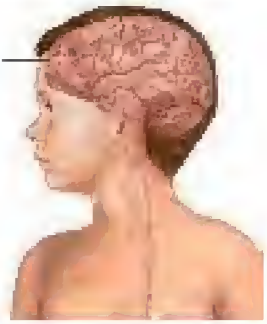
2. Gastrointestinal complications

1. Ulcerative stomatitis up to cancrum oris
2. Enterocolitis
3. Gastro enteritis

Measles may be complicated by malnutrition



3. Neurologic complications (Rare)
   - Viral encephalitis with a CSF pleocytosis
   - Acute disseminated encephalomyelitis during the recovery phase of measles
   - Subacute Sclerosing Panencephalitis(SSPE); slow virus infection which manifest years after measles attack
   - Guillian Barre syndrome
   - Aseptic meningitis.
   - Transverse myelitis



Others (Rare)
   - Myocarditis, DIC, thrombocytopenia

Prevention

- Measles vaccine at 9 months
- MMR vaccine 1st dose at 12-18 months
- MMR vaccine 2nd dose at 36 months (in USA at school age; 4- 6 years)

Treatment

a. For cases

Treatment is largely supportive; no specific therapy is of proven benefit

1. Supportive
   - Bed rest and isolation till rash disappear
   - Symptomatic e.g. eye care, paracetamol
   - Care of feeding : soft diet , fluids.
2. Treat complications e.g. Antibiotics for 2ry infection
3. WHO and UNICEF recommend single oral dose of vitamin A 100.000 - 200.000 IU to reduce measles morbidity for children with measles complications or at risk for complications

b. For contacts

- Exposed contacts with high risk of complications
  - This groups include infants < 1 year of age, and immunocompromised hosts
  - Intramuscular immune serum globulin can prevent measles if given within 6 days of exposure
  - Live vaccination is given 3 months later
- Exposed contacts without high risk of complications: can be given live measles vaccine within 72 hours of the exposure better than the immunoglobulin

(The American Academy of Pediatrics, the American Academy of Family Physicians, UpToDate website)

Rubella (German measles)

Etiology

- RNA virus One antigenic type, so, one attack gives lifelong immunity
- Transmitted by droplet infection/ Transplacental
- Incubation period 2-3 weeks
- Infectivity period 7 days before & 7 days after rash

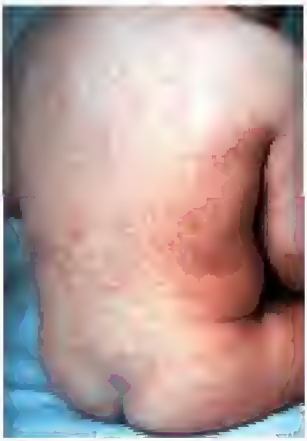
Clinical picture

a. Catarrhal stage

- Mild fever and mild nasopharyngitis
- Characteristic tender enlargement of posterior cervical & post auricular lymph nodes is ;appear 1day before the rash and last for up to 1 week

b. Eruptive stage

1. Fever /rash relationship
   - Rash appears on the 2nd day of fever.
   - Fever drops when the rash appear
2. Rash pattern
   - Maculopapular similar to measles's but less intensely red (*Rubella is a Latin word for "little red"*)
   - Starts in face then involve trunk & limbs
   - When reaches the trunk, it fades from the face
   - Fades on the 3rd day (3 days measles) without desquamation



Complications

- Congenital rubella syndrome if the mother catches infection during pregnancy especially in 1st trimester
- Other rare complications: Thrombocytopenia, encephalitis, and arthritis.

Prevention: MMR vaccine (see before)

Treatment

1. For cases : Symptomatic care
2. For exposed pregnant :Test immediately for maternal rubella Antibody IgG
   - If positive → she is immune →continue pregnancy with close follow up
   - If negative and remained negative in subsequent tests → infections hasn't occurred
   - If negative initially and turned up positive in subsequent tests either
     - Termination of pregnancy (Better and recommended)
     - If mother declined termination; rubella immune globulin may be given (may reduce severity of fetal infection) *(CDC and UpToDate 2012)*

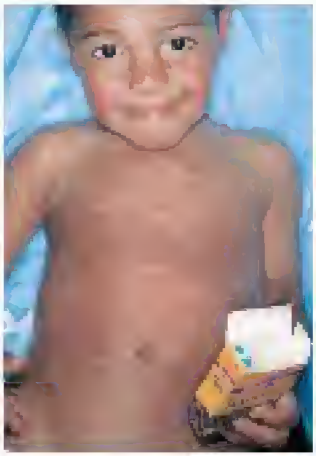
Roseola Infantum

Etiology

- Human herpes type 6 virus(DNA virus)
- Transmitted by droplet infection
- Incubation period: 5-15 days
- Peak age: 5-15 months(*Infantum*)

Clinical picture

1. **Fever /rash relationship**
   - Abrupt high fever up to 39-40 °C
   - Febrile convulsion is common
   - Fever fall by crisis at the 3rd – 4th day of illness
   - Rash appears 12-24 hours after fever's drop
2. **Rash pattern**
   - Maculopapular; rose-like rash (*Roseola*)
   - Starts on the trunk → then rise to involve neck, face & lower limb.
   - Rapidly fades in 2 days without desquamation



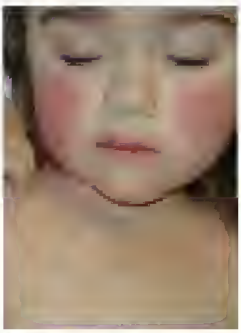
Treatment

- Symptomatic
- Ganciclovir for complicated cases (very rare)

Erythema Infectiosum

Etiology

- Human Parvo B19 virus (DNA virus)
- Transmitted by droplets infection and transplacental
- Incubation period 5-15 days



Clinical picture

- Mild catarrhal stage followed by
- Sudden livid erythema of cheeks (*slapped cheeks*)
- Maculopapular rash follows starting on the trunk
- The rash fades with central clearing (*lacy appearance*)

Complications

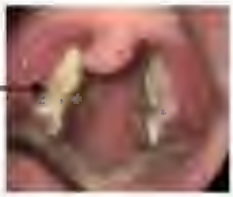
- Transient arthritis/arthralgia
- Erythroblastopenic crisis in patients with chronic hemolytic anemia

Treatment

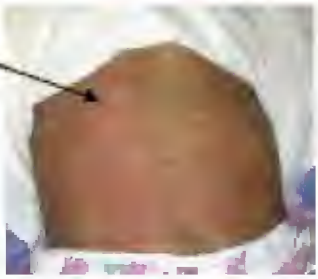
- Symptomatic
- IVIG for immunodificients and chronic hemolytic anemia patients

Infectious mononucleosis
(Glandular fever)

Etiology
- Epstein Barr virus (DNA, oncogenic virus)
- Transmitted by droplet infection and rarely blood borne
- Incubation period : 1 – 2 months
- The virus infect the epithelium then establish in B-lymphocytes

Clinical picture


- Fever , severe fatigue and sore throat
- Tonsillopharyngitis with thick white tonsilar membrane
- Lymphadenopathy(90%) commonly affect cervical group but may be generalized
- Maculopapular skin rash in 15% but in up to 80% of patients if ampicillin or amoxicillin are given
- Mild splenomegaly (50% of cases)
- May be hepatitis and hepatomegaly (10%)



Complications
- Upper airway obstruction by enlarged tonsils
- Rupture spleen; even with minor trauma
- Hematologic disorders: Aplastic anemia, auto immune hemolytic anemia and thrombocytopenia
- Pneumonia
- Myocarditis
- Oncogenicity e.g. nasopharyngeal carcinoma & Burkitt's lymphoma

Investigations
- Absolute lymphocytosis (lymphocyte count >4500/mm^3) & atypical lymphocytes >10%
- Positive heterophile antibody test ; antibodies that agglutinate sheep RBCs (Paul Bunnell test) or horse RBCs (Monospot test)
- EBV IgM antibody or EBV capsid antigen only for heterophile test negative

Treatment
- Symptomatic treatment: antipyretics (avoid aspirin) and bed rest
- Avoid contact sports in the first 2-3 weeks (to avoid rupture spleen)
- Steroids for: - Tonsillar enlargement with upper airways obstruction
  - Auto immune hemolytic anemia and thrombocytopenia
  - Seizures and meningitis
- Treatment of complications

Differential Diagnosis of Maculopapular Rash

1. **Viral Exanthema e.g.**
   - Measles
   - Rubella
   - Roseola infantum
   - Erythema infectiosum
   - Infectious mononucleosis.
2. **Bacterial Exanthema e.g.**
   - Scarlet fever
   - Typhoid fever
   - Meningococcaemia (Toxemia, blood culture, CSF examination)
3. **Ricketssial infections**
4. **Collagen vascular disorders**
   - Kawasaki disease
   - Systemic lupus erythematosus
   - Systemic onset rheumatoid arthritis
5. **Allergic**
   - Serum sickness and drug eruption : History of drug intake ,itching
6. **Insect bites** (e.g. fleas) → Itching ; insect may be seen
   → Lesions fade on pressure.

Kawasaki Disease (KD) : Vasculitis of medium and small-sized blood vessels

Diagnostic criteria

- Prolonged unexplained fever of >38. 5°C ≥ five days plus at least 4 out of:
  - Bilateral non exudative conjunctivitis
  - Mucositis: cracked, red lips , a strawberry tongue and injected pharynx
  - Polymorphous rash: perineal erythema, followed by macular, morbilliform, or targetoid skin rash of the trunk and extremities
  - Extremity changes: edema of the dorsum of hands and feet, and a diffuse erythema of palms and soles
  - Cervical lymphadenopathy; at least one lymph node >1.5 cm in diameter.
- KD carries risk of coronary aneurysms and infarction

Investigations

- Elevated acute phase reactants and thrombocytosis
- Echocardiography follow-up for coronary aneurysms

Treatment

- IVIG 2gm/kg IV infusion over 8-12 hours
- Aspirin oral 80-100 mg/kg till fever decline for 48 hours then antiplatelet dose 3-5mg/kg till acute phase reactants normalizes

Self assessment case scenarios

Case 6

A 17-month-old nonimmunized girl has had fever for 4 days and coryzal manifestations followed by a maculopapular rash. Once she developed the rash, the temperature shoots to 40 C for 2 days. Throat examination showed grayish white spots over the inner aspect of the cheek. There is a 4-month-old sibling at home.

What is the appropriate management for this sibling?

Case 7

A pregnant mother in the 1st trimester brought her 8 years old girl who had fever and mild coryzal manifestations for 2 days. Fever immediately settled the time a skin rash appeared. On examination the girl was entirely normal apart from faint rosy maculopapular rash over the face and upper chest along with tender bilateral post auricular lymph nodes

a. **What exanthema disease does this girl have?**
b. **What is the appropriate advice for her mother?**

Case 8

14-year-old girl presented with a one-week history of fever38 C, sore throat, progressive fatigue, malaise with mild bilateral posterior cervical adenopathy. Sclera jaundice was prominent. The abdomen was remarkable for moderate hepatomegaly and splenomegaly. Laboratory findings revealed hemoglobin 12 g/dL; platelet count 69.000/mm^3; white blood cell count 8.400/mm^3 with 10% atypical lymphocytes. Liver function tests reported AST 368 IU/L; ALT 319 IU/L, albumin 3.3 g/dL. Total bilirubin was 4.0 mg/dL and direct bilirubin was 2.4 mg/dL

a. **What are the most important 4 investigations?**
b. **What is the diagnosis?**

Case 9

This is a 5 year old male who is referred to your clinic by the school nurse for suspicion of child abuse because the child's face appears to have been "slapped" repeatedly. The child has been checked up regularly and is up to date on immunizations. On examination; Temperature is 38.2 C , slight erythema of his oropharynx and pinkish red color of his cheeks. Further questioning reveals an ill cousin with a "rash." Over the next several days, the malar erythema begins to fade and a faint pink rash appears on his trunk and extensor surfaces of his upper extremities. The truncal rash becomes confluent, creating a lacy appearance. Both the fever and rash disappear without any further problems

a. **What is your diagnosis?**
b. **What is the etiology?**

Chicken pox
(Varicella)

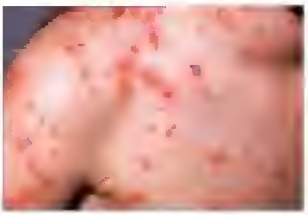
Etiology

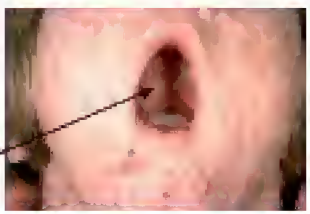
- Varicella Zoster Virus(VZV): DNA human herpes virus which can cause varicella in children and Herpes Zoster (shingles) if reactivated
- Transmission : - Droplet infection from cases
  - Contact with skin lesions from cases
- Incubation period: 2-3 weeks
- Patients are infective 2 days before the rash and till the rash crusted

Clinical picture

- **Prodroma**
  - Fever, malaise, anorexia may occur 24-48 hours before the rash
  - These symptoms resolve within 2-4 days after the onset of the rash
- **Rash**

Appear first	- On the scalp, face, or trunk
Distribution	- Centripetal with little involvement of the limbs
Pattern	- Erythematous macules → evolve into papules → vesicles (tear drop on a base of erythema) → crusts (and pustules may form)
Characteristics	- Simultaneous presence of lesions in various stages - Very itchy rash - In mucus membranes → vesicles may ulcerate

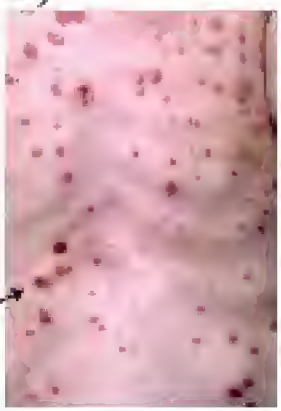




Complications

1. Secondary bacterial infection of the vesicles (in 5% of cases)
2. Progressive varicella may occur in
   - Adolescents and adults even healthy !
   - Immunocompromised children
   - Newborns

   Manifestations
   - Visceral organs involvement
   - Coagulopathy , and severe hemorrhage
   - Hemorrhagic vesicles(*Hemorrhagic varicella*)
   - Severe abdominal pain(involved mesenteric lymph nodes or the liver)
   - Fatal course if adrenal hemorrhage occur



(American academy of pediatrics)

3. Other rare complications
   - Mild thrombocytopenia and transient petechiae may occur in 1-2 %
   - Rye's syndrome ; especially with concomitant Aspirin
   - Meningoencephalitis and cerebellitis→ transient cerebellar ataxia
   - Viral pneumonia
   - Viral myocarditis
4. Congenital varicella
   - If pregnant mother catches infection in the first trimester
   - Clinically: Low birth weight , mental retardation &congenital anomalies

Treatment

1. **Prevention**: *Chicken pox Vaccine*
   - Live attenuated vaccine.
   - Given at 12-18 months age
   - Dose: - Single dose between 12 months to 12 years.
     - Above 12 years → 2 doses 4 weeks apart
   - Protective value up to 95%.

2. **For cases**

a. General
- Antipruritic : calamine lotion , anti histaminics
- Antipyretic (paracetamole); never use aspirin.
- Antibiotics for 2ry bacterial infection

b. Antiviral

Acyclovir	20 mg/kg/dose, given 4 doses per day, for 5 days
Value	Modify clinical picture and prevent complications
Indications	Children >12 mo of age: - With chronic cutaneous or pulmonary disorders - Receiving short-term, intermittent, or aerosolized corticosteroid therapy, - Receiving salicylate therapy
Non indication	Not recommended routinely in the healthy child
Initiation	As early as possible, preferably within 24 hr of the onset of the rash

(American Academy of Pediatrics)

3. **Post exposure prophylaxis**

a. Chicken pox vaccine
- Given to healthy children within 3-5 days after exposure
- Effective in preventing or modifying varicella especially for household contacts and for outbreak control.

b. Anti-VZV immune globulin

- Recommended for post exposure prophylaxis for:
  - Immunocompromised children
  - Pregnant women
  - Newborns
- Dose is 1 vial (125 units) for each 10-kg of body weight ,IM
- As soon as possible but within 96 hr after exposure.

c. Oral acyclovir: late in the incubation period may be protective (??)

Differential diagnosis of papulo vesicular rash

1. Viral infections
   - Chicken pox
   - Herpes zoster (reactivation of dormant varicella)
   - Herpes simplex
   - Hand, Foot, and Mouth Disease
2. Impetigo contagiosa
3. Scabies
4. Others: Fungal infections, Insect bites, Drug eruption

Hand, Foot, and Mouth Disease

- Caused by Coxachie A virus (an Entero virus)
- Transmitted by oral-oral or fecal-oral routes
- Clinically
  - Oral mucosal lesions : macules or small vesicles that evolve to painful ulcers
  - Palms or soles lesions: Red macules or papules appear in a linear arrangement. They quickly evolve to form vesicles with a clear, watery appearance
- Management
  - Symptomatic e.g. topical local anesthetics to reduce oral discomfort
  - A diet of vanilla ice cream is the easiest to tolerate

Self assessment case scenarios

Case 10

7 years old child was brought to the hospital because of vomiting, lethargy, slurred speech, and difficulty in walking. The patient had been in excellent health until 2 days before admission. His brother had had varicella 2 weeks previously. The physical examination at admission revealed an irritable but cooperative child. A neurological examination revealed no abnormality except for nystagmus upon lateral gaze to either side. His skin shows corps of vesicles and papules mainly on the trunk

a. What is the initial disease?
b. What is the complication?
c. What is the prognosis?

Case11

An 18-month-old child presents to your office with a 2-day history of fever. He is not eating well and the mother tells you that she thinks his mouth hurts. On examination you see 3 mm vesicles on erythematous bases on the soft palate and tonsils. The child also has small vesicular lesions on his palms and soles

a. What is the diagnosis?
b. What is the etiology?

Mumps
(Epidemic Parotitis)

Etiology

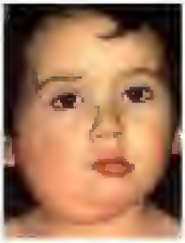
- RNA paramyxo virus affecting the salivary glands.
- Transmission: Droplet infection from human cases; no carriers.
- Incubation period: 2-3 weeks.

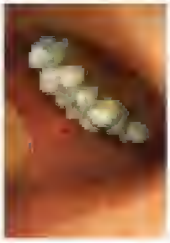
Clinical picture

- About 25-30% are subclinical
- Prodroma ; mild fever, malaise & myalgia
- Acute non suppurative inflammation of salivary glands

a. Parotid gland

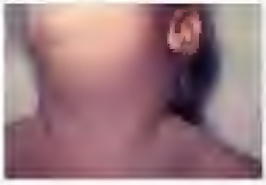
- Usually one side precede the other
- Tender parotid swelling → push the ear forward and outward
- Swelling ↑ by teeth clinching and ↓ by mouth opening.
- Hyperemic stenson duct orifice
- Swelling ↑ to maximum over 3 days and ↓ over 5 days





b. Submandibular gland

- Submandibular swelling
- May be with parotitis (Alone in 10 %)
- Less painful



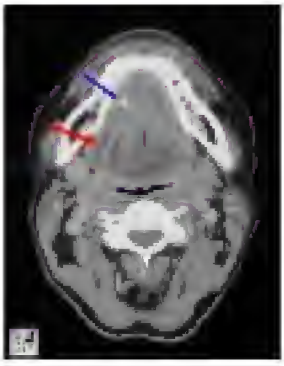
c. Sublingual gland

- Least common
- Submental swelling
- May be with chest wall edema

Differential diagnosis

1. Parotid stone (acute obstructive parotitis)

- Pain increase by mastication.
- Stone may be felt under the skin
- Stone can be detected by X-ray or CT
- Swelling may be intermittent.



2. Parotid abscess

- Mainly due to staph aureus.
- High fever.
- Throbbing pain.
- Pus may ooze from Stenson duct orifice.

3. Endemic parotitis

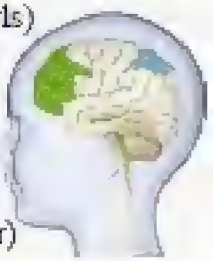
- Bilateral painless swelling of parotids
- Due to malnutrition, ankylostoma, chronic anemia

4. Upper deep cervical lymphadenitis

Complications

1. Meningitis and Meningoencephalitis

- The most frequent complication (10 - 30 % cases; boys > girls)
- Most commonly manifests 5 days after the parotitis
- Clinically
  - Fever, vomiting, headache ,and convulsions
  - Meningeal irritation signs in older children
  - CSF (clear,↑tension,↑protein,↑lymphocytes, normal sugar)
  - In typical cases, symptoms resolve in 7-10 days
  - Aqueduct stenosis and hydrocephalus are rare possible sequels

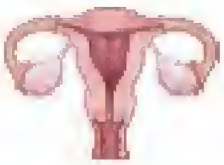


2. Epidydimo- Orchitis

- Commonest complication in adolescents boys and adults
- Usually follow parotitis
- Clinically
  - Fever, chills ,lower abdominal pain
  - Severe testicular pain, accompanied by swelling and erythema of the scrotum
  - Usually unilateral (Bilateral in ≤ 30%)
  - Atrophy of the testes and impaired fertility may occur but sterility is very rare even with bilateral involvement

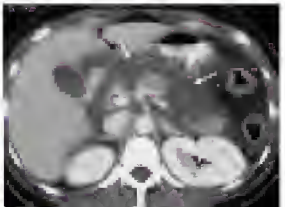
3. Oophoritis

- Uncommon in post pubertal girls
- Clinically
  - Pelvic pain and tenderness
  - May be confused with appendicitis when located on the right side



4. Acute hemorrhagic pancreatitis

- May occur even without parotid swelling
- Features
  - Acute epigastric pain and tenderness
  - Vomiting, fever &prostration
  - ↑ serum lipase is characteristic
  - Abdominal ultrasound and CT scans are diagnostic



5. Other rare complications

- Sensorineural hearing loss
- Thyroiditis
- Myocarditis
- Migratory polyarthralgia
- Mumps emberyopathy(abortion or enocardial fibroelastosis of fetal heart)

Treatment

a. Prevention
   - MMR vaccine (see before)

b. Cases
   - Isolation: Patients with mumps should stay home from school or work for five days after onset of clinical symptoms, as recommended by the American Academy of Pediatrics (AAP)
   - Symptomatic treatment:
     - Topical application of warm or cold packs to the parotid gland may be soothing
     - Analgesics e.g. acetaminophen
     - Soft diet (avoid sour fluids)
   - Treatment of complication e.g.
     - Orchitis (support testis ,analgesics)
     - Acute pancreatitis responds to supportive care (IV fluids,electrolytes)
   - The local public health officials should also be notified .

Case 12

A 17-year-old male patient was admitted to the emergency unit with nausea and vomiting. On physical examination, the patient was unconscious, had neck stiffness, his temperature was 38°C, his blood pressure was normal; he had bilateral swellings in the parotid regions and findings of unilateral red swollen scrotum

a. **What is the diagnosis?**
b. **What is the required investigations?**
c. **What is expected from his lab investigation?**

Case 13

A 17-year-old male patient was admitted to the emergency unit with nausea and severe vomiting associated with a band-like back pain, shortness of breath, and palpitation. On physical examination, pulse 195 bpm,he had bilateral swellings in the parotid regions Blood glucose 192 mg/dl , amylase 512 u/l (n 25-125), CPK 1121 u/l (n 38-174), and CK-MB 75 u/l (n 2-6)

a. **What is the diagnosis?**
b. **What are the most important investigations?**

(Indian Journal of Radiology and Imaging, 2006 ,Volume : 16, Issue : 3, Page : 305-308)

Poliomyelitis

Causes

- RNA enterovirus with 3 serotypes (I, II, III)
- Transmission: Faeco oral infection or droplet infection
- Outcome of infection
  - Not all infected cases develop the disease
  - Incidence is 1 diseased for 10.000 infected depending on
    - Neurovirulence of the virus
    - Host factors e.g. Extremes of age ,I.M injection

Pathology of the disease

- Damage to the motor nuclei in spinal cord (anterior horn cells) and brain stem → atrophy of muscles supplied by these motor cells.
- Encephalitis may develop in some cases.

Clinical Forms

Listed in order of severity

1. Subclinical infections
2. Abortive poliomyelitis (minor illness)
   - The commonest form (80-90%) with mild constitutional manifestations.
   - Presentation : Mild fever, rhinitis , sore throat Or Abdominal pain and ,diarrhea
3. Non paralytic poliomyelitis

As abortive plus picture of aseptic meningitis

- Muscle tenderness
- Meningeal irritation: Pain & stiffness in neck, back & extremities
- Tripod sign : ask the baby to sit ; there will be 3 points of support ; buttocks, hands behind & feet in front
- Head drop sign ⇒ If the baby lifted ⇒ head drops backwards due to weak neck muscles
- Urine retention due to bladder paralysis

4. **Paralytic poliomyelitis:**

Characters of paralysis

- Lower motor neurone ⇒ hypotonia, hyporeflexia with muscle wasting
- Asymmetric ⇒ one limb is affected more than the other.
- Patchy distribution ⇒ affect some groups (esp. the large) sparing others in the same limb.

Types of paralysis

- Spinal
  - 2ry inability to walk (lower limb muscles)
  - Respiratory failure (respiratory muscles)
  - Scoliosis (trunk muscles)
- Paralysis of medullary nuclei
  - Cranial nerves 9,10,11,12 → Palato-pharyngeo-laryngeal paralysis
  - Respiratory center→ irregular breathing
  - Vasomotor center →labile blood pressure and dysrhythmias

Diagnosis

Viral isolation Stool Throat

Differential diagnosis

A. Causes of acute flaccid paralysis:

Paralytic disease	Features of paralysis
Guillian Barre syndrome	Symmetric , ascending , motor &sensory
Tick paralysis	Symmetric , ascending , / find the tick
Post diphteritic	Symmetric , descending, motor & sensory
Botulism	Symmetric , descending / history
Transverse myelitis	Symmetric , non progressive , with sensory level

B. Causes of pseudo paralysis

- Bones: scurvy, osteomyelitis and fractures
- Joints: arthritis, dislocation and synovitis

Management

Prevention: Polio vaccines

Supportive

- Analgesics (avoid injections).
- Bed rest with good diet.
- Care of bladder (parasympathomimitics ± catheter)
- Care of comatosed
- Decrease deformity by proper positioning of limbs.
- Enema and laxatives for constipation
- Physiotherapy after 2-3 weeks & orthopedic consultation

Treat complications

- For Bulbar paralysis:
  - Support respiration
  - Monitor blood pressure
  - Care of nutrition

Parasitic Diseases

Nematodes

- Ascaris
- Enteroblius vermicularis

} Infection occur by. Ingestion of eggs.

- Ankylostoma (hook worm)
- Strongyloids

} Infection occur by. Skin penetration by larvae.

Clinical features

- Asymptomatic
- Abdominal pain
- GIT bleeding (anemia).

} Malnutrition and impaired growth may occur

- In Ankylostoma & Strongyloids → skin penetration may lead to → pruritic maculopapular rash at the site of penetration (Ground itch)
- Ascaris &ankylostoma may lead to pulmonary symptoms due to larval migration
- Ascaris may lead to intestinal obstruction.
- Enterobius (oxyuris) may lead to:
  → Enuresis & irritability
  → Nocturnal anal pruritus

Diagnosis

- Detect the worm or the characteristic eggs in stool.
- Test for complications: occult blood in stool, iron deficiency anemia.

Treatment

- General: hand washing, fingernails kept cut &clean, avoid bare footing.
- Albendazole (400 mg PO once) or Mebendazole or Flubendazole 100 mg twice daily for 3 days
- For oxyuris
  - Single oral dose of Mebendazole (100 mg) or Albendazole (400 mg)
  - Repeat in 2 weeks with treatment of all family contacts
- Nitazoxanide (100-200 mg bid PO for 3 days)give same cure rate as Albendazole
- Ivermectin (Stromectol, Mectizan) is FDA approved for treatment of intestinal Strongyloids

Schistosomiasis

Life cycle

Exposure to water channels → cercariae penetrate skin which mature into adult worms in 1-3 months which travel to:

- Urinary bladder→ Schistosoma heamatopiuin
- Intestine →Schistosoma mansoni

Adult worms lay eggs when eggs reach fresh water they inhabit the snails to mature into hundreds of cercariae

	Schistosoma heamatopium	Schistosoma Mansoni
Incidence	- Prevail in all Egypt	Prevail in lower Egypt
Clinical picture	Pruritic papular dermatitis may occur at site of cercarial entry	
	- Cystitis - Terminal heamaturia - Late ⇒ cancer bladder	- Bleeding per rectum - Abdominal pain , diarrhea , tenesmus - Late : liver fibrosis & portal hypertension
Investigation	- Urine analysis for ova - Rectal snip& look for ova - Serology is not accurate	- Stool analysis for ova - Bladder biopsy& search for ova - Serology is not accurate
Treatment	Praziquantel 40 mg/kg/d in 2 divided oral dose (drug of choice)	

Cestodes

	T. saginata	T. solium	H. Nana
Definitive host	Human	Human	Human
Intermediate host	Cattles (beef)	Pigs (pork)	Fleas
Infection	Ingestion of cysticercus bovis in under cooked beef	Ingestion of cysticercus cellulosa in under cooked pork	Ingestion of eggs
Clinical picture	- Abdominal pain - Distension - Weight loss	- Abdominal pain - Distension - Weight loss	- Abdominal pain - Distension - Weight loss - Irritability & fits due to neurotoxins
Treatment	Praziquantel 25 mg /kg single oral dose or Niclosamide : 50 mg/kg PO once for children, 2 g PO once for adults However, this medication is no longer available in the USA		

Ecchinococcus granulosus

Definitive host Dogs
Intermediate host Humans and Cattle
Clinical picture Eggs change into cysts into the liver(2/3) , lungs, brain→ compression manifestation
Rarely cyst rupture → severe anaphylaxis
Treatment
- High dose Albendazole for 6 months
- Surgical removal or ultra sonic aspiration for severe pressure manifestations

Diseases Caused By Protozoa

	Amoebiasis	Giardiasis
Etiology	Entamoeba histolytica	Giardia lamblia
	* Inhabit the large intestine. * Exist in two forms: - Cystic form (non invasive) - Vegetative form (invasive).	* Inhabit the upper small intestine * Present in two forms : - Cyst form (non invasive) - Vegetative form (invasive).
Transmission	Feco-oral route	Feco-oral route
Clinically	- Asymptomatic. - Amoebic dysentery - Extra intestinal (Lung & liver abscess)	- Asymptomatic. - Diarrhea - Abdominal distention - Abdominal pain (chronic, recurrent). - May be malabsorption syndrome
Treatment	Asymptomatic intestinal carriers Paromomycin or Diloxanide furoate oral in 3 dose for 7 days Invasive forms ○ Initial Metronidazol 50 mg/k/day (oral 3 doses) for 7-10 days or Tinidazol 50 mg/k/day (oral single dose) for 3 days ○ Followed by 7 days course of oral Paromomycin 25 mg/kg/day	Prefered ▪ Tinidazole 50 mg/k/d single dose ▪ Nitazoxanide 4-11 yr: 200 mg bid for 3 days >12 yr: 500 mg bid for 3 days ▪ Metronidazole 15 mg/k/d for 7 days Alternative ▪ Albendazole 400 mg once a day for 5 days

Fever

Definition

- A rectal temperature ≥38°C
- A value >40 °C is called hyperpyrexia.
- Any abnormal rise in body temperature should be considered a symptom of an underlying condition

Etiology

- **Infectious:**
  - Self-limited viral infections (common cold, gastroenteritis) and uncomplicated bacterial infections (otitis media, pharyngitis, sinusitis) are the most common causes of acute fever
  - Others: urinary tract infections, pneumonia, meningitis,…
- **Inflammatory** e.g. Rheumatic diseases
- **Neoplastic** e.g. Leukemia and Neuroblastoma
- **Miscellaneous** e.g. Familial Mediterranean Fever

Evaluation of acute fever

- Thorough history: onset, other symptoms, exposures (daycare, school, family, pets, playmates), travel, medications, other underlying disorders, immunizations
- Physical examination: complete, with focus on localizing symptoms
- Laboratory studies on a case-by-case basis
  - Rapid antigen testing
    - Nasopharyngeal: respiratory viruses
    - Throat: group A streptococcus
    - Stool: rotavirus
  - Throat culture
  - Blood: complete blood count, blood culture, C-reactive protein, sedimentation rate
  - Urine: urinalysis, culture
  - Stool: hemocult, culture
  - Cerebrospinal fluid: cell count, glucose, protein, Gram stain, culture
- Chest radiograph or other imaging study

(Nelson textbook of pediatrics)

Fever without focus

Definition

Fever without a focus refers to a rectal temperature of 38°C or higher as the sole presenting feature

Categories

1. Fever of unknown origin
   Children with fever documented by a health care provider and for which the cause could not be identified after 3 wk of evaluation as an outpatient or after 1 wk of evaluation in the hospital
2. Fever without Localizing Signs
   Fever of acute onset, with duration of <1 wk and without localizing signs

Fever without localizing focus

Common causes

- Viral infection
- Occult bacteremia
- Bacterial infections e.g.
  - Ear infection
  - Urinary tract infections
  - Meningitis
  - Pneumonia
  - Osteomyelitis
  - Septic arthritis

Management

Hospitalize

- Neonates
- Any toxic child

Medical history for

- Appetite
- Activity
- Reactivity to others
- Recent contact with diseased
- Immunization history

Physical examination for

- Look: normal /active (? viral illness) or sick/inactive (? bacterial illness)
- Color and perfusion

- Level of arousal
- Cry quality

Investigations

a. CBC for leucocytosis(>15000 cell/mm^3) , bandemia (band cells >20%) or leucopenia (<5000 cell/mm^3) usually indicate bacterial infections
b. C reactive protein(CRP) usually negative in viral infections
c. Urinalysis for leukocyte esterase, nitrite and pyuria (>10 WBC/HPF)
d. Stool analysis for cases with diarrhea
e. Cultures (urine, stool, blood, CSF)
f. Chest X ray for any infiltrates

Start empiric antibiotics for

1. Neonates
2. Toxic children
3. Young children who have not received Hib and *S. pneumoniae* vaccines and who have a rectal temperature of >39°C and leucocytosis

Compulsory Vaccines

	BCG	Oral polio vaccine	DTaP	Hepatitis B vaccine	Measles vaccine
Nature	Live attenuated T.B bacilli (bacilli of Calmette & Gaurin)	Trivalent live attenuated polio virus types 1,2,3 (Sabin vaccine)	Diphteria & tetanus toxoids with acellular pertussis vaccine (DPT is no longer used)	Recombinant HBs Ag prepared by DNA technology.	Live attenuated measles virus grown in chicken embryo cell culture.
Indications	Compulsory Vaccination Started during the 1st year of life			- Chronic blood recipients - IV drug abusers - Hemodialysis patients.	
Administration	0.05 ml in neonates 0.1 ml in elders Intradermal in left upper arm.	3 drops oral	0.5 ml I.M in left thigh	- 0.5 ml before 10th year. - 1 ml afterwards. IM (in left thigh/deltoid)	- 0.5 ml S.C in upper right arm
1ry doses	In the 1st 3 months	Zero dose at 0-15 days. 2,4,6 months	2,4,6 months	2,4,6 months (in other conditions 0,1,6 months).	9 months
Booster doses	At beginning of every school period for tuberculin –ve	- At 18 months - At 4 years (frequent doses is recommended)	- at 18 months - at 4 years(DT)		As MMR at 12-18 months and again at 4-6 years
Reaction	Small papule which crust then disappear in 8-12 weeks leaving permanent scar.	No reaction, has many values; - Low cost - Give both local & humoral immunity. - Virus excreted in stool → transmitted to others → community immunity.	- Fever - Local tenderness - Irritability and crying for > 3 hours. - Shock like; hypotonic hyporesponsive episode - Convulsions - Encephalopathy.	- Local reaction : pain tenderness, swelling & erythema. - Fever - Headache	- Mild fever - Faint skin rash may occur 1-2 weeks after vaccination → last for 1-2 days.

	BCG	Oral polio vaccine	DTaP	Hepatitis vaccine	Measles vaccine
Complications	• Regional (axillary) lymphadenitis ⇒ need INH • Abscess formation • Dissiminated infection if given to immunodef. Or improper attenuation ⇒ need anti- TB. Drugs.	• Failed vaccine due to - defect storage - vomiting or diarrhea • Vaccine associated paralytic polio (incidence: 1/ 750.000)	Severe previous reaction (usually due to pertussis vaccine)	• Failed vaccine due to:- defect storage - injections in buttocks	• Encephalitis.
General contraindications and precautions ✧ **Contraindications to all vaccines** - Serious allergic reaction (e.g., anaphylaxis) after a previous vaccine dose - Serious allergic reaction (e.g., anaphylaxis) to a vaccine component ✧ **Precautions**: Moderate or severe acute illness with or without fever			✧ **Contraindications to live virus vaccines** - Immunosuppressed patient (immunosuppressive therapy or diseases) - Malignancy - Pregnant mother		
Additional contraindications	• Tuberculin +ve reactors • Prematures.	• Immunodeficient contacts • In nurseries	See later	See later	See later
Other forms		Inactivated polio vaccine (Salk) * Dose ⇒ 0.5 ml S.C. * Given if sabin vaccine is contraindicated * Dose of Salk before OPV reduce OPV associated paralysis by 90%	TdaP and Td contain reduced dose diphtheria toxoid to be given as boosters to adolescents when pertussis vaccine is unnecessary		MMR vaccine is live attenuated vaccine for mumps, measles & rubella 0.5 ml S.C.

Specific contraindications and precautions to commonly used vaccines

Vaccine	True contraindications and precautions
DTaP	**Contraindications** - Encephalopathy (e.g., coma, prolonged seizures) - Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy. (Decision: defer DTaP until neurologic status stabilized) **Precautions** - Fever of > 40.5 °C ≤ 48 hours after receiving a previous dose - Shock like state ≤ 48 hours after receiving a previous dose - Seizure ≤ 3 days of receiving a previous dose - Persistent crying lasting ≥ 3 hours ≤ 48 hours after receiving a previous dose .
MMR	**Contraindications** - Pregnancy - Known severe immunodeficiency . **Precautions** - Recent (≤ 11 months) receipt of antibody-containing blood product - Thrombocytopenia
Hepatitis B	**Contraindication** - Pregnancy - Autoimmune disease (e.g., systemic lupus erythematosis) **Precautions** - Infant weighing < 2,000 grams

(Current Pediatrics textbook)

Other Vaccines (Non Compulsory in Egypt)

General indications: - High risk patients - Household contacts - Travelers to endemic areas

Vaccine	Nature	Dosage (0.5 ml)	Other indications /notes
Heamophilus influenza type B (HiB) vaccine	Antigenic part of the capsule	- I.M.	• Hyposplenism
		- at 2,4,6 months	• Prior to splenectomy
		- booster dose at 15 mo.	• Resistant nephrotic syndrome
Polyvalent pneumococcal vaccine	Capsular polysaccharide of 23 serotypes	- I.M.	
Meningeoccocal vaccine	Purified capsular polysaccharide of types A, AC, C, W135	- S.C (local erythema is a common side effect)	- Hyposplenism - Prior to splenectomy
Hepatitis A (Havrix)	Inactivated	- I.M.; 2 doses 6 months apart - Given above 1 year	
Typhoid vaccines			Drawbacks : - Short period of effectiveness Fever , headache , malaise
1- Vi capsular vaccine	Conjugated vaccine	- I.M single dose - Given above 2 years	
2- TY 21a	Live attenuated	- Oral single dose.	
3- TAB vaccine	Heat phenol inactivated	- ¼ ml SC ; 2 doses 1 mo. apart	
Influenza vaccine*	Inactivated viruses	- IM 2 dose 1 month apart - Common type for season	* Chronic lung diseases * Patients on long term aspirin.
Chicken pox vaccine	Live attenuated	- SC → single dose (< 12y) → 2 doses (> 12 y)	* Patients on long term aspirin

* Influenza vaccine may be complicated with fever , local reactions and Guillian Barre syndrome

Rota virus vaccine

- Live attenuated, given orally; 2.5 ml/dose for two doses 4 weeks apart Efficacy: 70 %
- The first dose must be before 3 months and final dose must be before 6 months

* Complications: loose stool and low grade fever
* Avoided in gastro enteritis, immunodeficiency, anaphylaxis and beyond 6 months

Neonatology

Neonatal Resuscitation

Definition

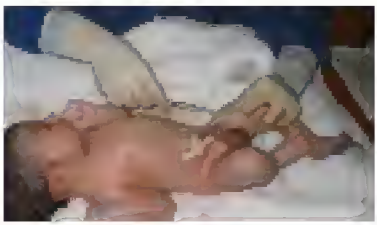
Immediate steps done to optimize newborn airway, breathing & circulation after birth

Resuscitation steps

- Receive the baby in a pre warmed towels and dry thoroughly
- Quick evaluation of the infant by Apgar scoring
  - * At 1 minute → Reflects the need for and method of resuscitation.
  - * At 5 minutes → Reflects adequacy of resuscitative efforts.
  - → More precisely predict the neurologic outcome

Sign	0	1	2
Color (Appearance)	Blue or pale	Pink with blue extremities.	Completely pink.
Heart rate (HR; Pulse)	Absent	Under 100 / min	over 100 / min
Response to nasal catheter (Grimace)	No response	Grimace	Cough, sneezing.
Muscle tone (Activity)	Limp (flaccid)	Some flexion	Well flexed
Respiration	Absent	Slow , irregular	Normal and crying

Action plan



A. Crying baby with good tone (Scores of > 7)

- Keep warm, Care of the cord and IM Vitamin K
- Deliver to the mum or admit if indicated

B. Apneic, Flaccid, HR<100 (Scores of < 7)

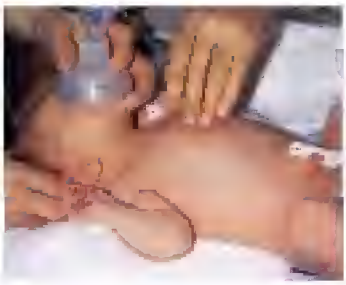
- Dry well and keep warm under radiant warmer
- Reposition the neck in neutral position and Clear airway as necessary

Reassess Breathing, HR and color every 30 seconds

- If breathing & HR > 100 bpm but central cyanosis → Supply oxygen as needed
- If apnea (floppiness) , HR < 100 bpm and /or persistent central cyanosis

1. Ensure the baby is dry, warm and the airway is patent
2. Call for help! And
3. Provide positive pressure ventilation (PPV):
   - Five inflation breaths at 30 cmH_2O followed if necessary by ventilation breaths at 25 cmH_2O for 30 seconds
   - Using bag and face mask or Neopuff

Reassess after 30 seconds of effective ventilation



- If HR < 60 bpm→ PPV (via endotracheal tube) + Chest compressions at rate of 3:1 with PPV

Reassess after 30 seconds of effective ventilation and cardiac massage

HR remains < 60 bpm after 1-2 min

heart rate > 60 bpm and rising → stop cardiac massage and continue PPV till spontaneous respiration is regained

Insert umbilical venous catheter and:

- Send sample for pH, blood gases, Hb and glucose
- **Give Adrenaline**
  - Dose: 0.1 – 0.3 ml/kg of 1:10.000 solution.
  - Route: intravenous or intra tracheal.

Reassess after 30 seconds of effective ventilation and cardiac massage

If no improvement

- Give a second dose of **adrenaline**
- **Sodium bicarbonate** 2 meq/kg slow I.V for documented metabolic acidosis or if 2 doses of adrenaline were ineffective
- Push 10-20 ml/kg saline IV (or O negative packed red cells if perinatal blood loss suspected or Hb% is low)

Further care include

- Cardiopulmonary monitoring
- Mechanical ventilation or assisted ventilation
- Surfactant therapy
- Move to NICU

Self assessment case scenarios

Case 1

You are attending delivery of full term baby delivered by elective caesarean section, baby delivered cyanosed, no respiratory efforts, extremities semiflexed, heart rate 110 bpm and no response to suction catheter

a. What is the estimated Apgar score?

You started resuscitation with drying , warming, clearing airways and you gave 5 inflation breaths, within few seconds the baby's color turned pink, crying with good tone and cough for any further suctioning

b. What is Apgar score now?

c. Does this baby have perinatal asphyxia?

Case 2

A woman is admitted on to delivery suite at term. Fetal heart rate monitoring was abnormal with marked decelerations to 40 and baseline bradycarida. She is taken immediately to theatre for emergency caesarean section, and the baby is born 15 minutes later. At delivery the baby is white, floppy and the heart rate is very slow

a. What are your first actions?

There is no respiratory effort, the heart rate is 20 bpm and the baby is white and floppy

b. What are the next four steps?

The chest is seen to move well, however the heart rate remains at <20bpm and the baby is still white and floppy

c. What are your next actions?

The baseline heart rate remains around 20bpm. Good chest movements continue. You insert an umbilical venous catheter

d. What is the first thing you will do after successful placement?

Heart rate remains slow and you decided to give resuscitation drugs

e. What will you use first?

f. How much you will give?

Blood tests you send from umbilical venous blood are reported back as:

Profound metabolic acidosis and hemoglobin 13.5 gm/dl .

g. What two actions you will consider?

h. What further care you will do for the baby?

(Source: Neonatology For MRCPCH and Beyond)

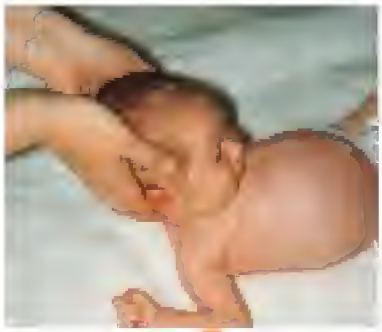
Primitive Reflexes

Idea

- Primitive reflexes are automatic stereotypic movements directed from the brainstem and require no cortical involvement
- They are needed for survival and development in the early months of life
- As the higher cortical centers begin to mature → successive disappearance of these reflexes take place allowing proper neurological development

Moro (Startle) Reflex

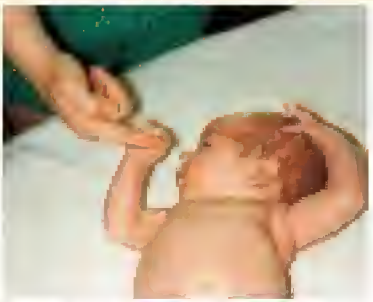
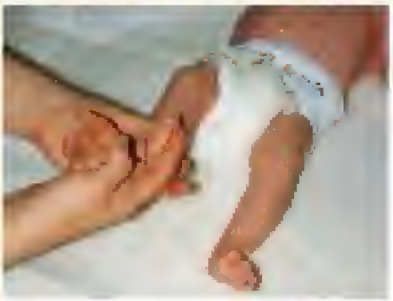
- Present at birth and disappears by 5- 6 months of age
- Start to develop intrauterine at 32 weeks and fully mature at 37 weeks
- Stimulus
  - The head is gently lifted then released suddenly into examiner's hand (avoid in preterm & suspected intra cranial hemorrhage)
  - Sudden withdrawal of the blankets from underneath the infant
  - Making a loud noise near the ear



- Response
  - Extension of the trunk
  - Extension and abduction of the arms with "fanning" of the fingers followed by flexion and adduction "as if the infant embraces himself "
  - Loud crying may follow

- Clinical value
  - Normal reflex in the normal time frame →Normal neurodevelopment
  - Abnormal reflex
    - Sluggish in sedated newborn and sepsis
    - Exaggerated in early kernicterus
    - Unilateral (asymmetrical) in Erb's palsy, fracture clavicle or humerus
  - Absent reflex (two sided)
    - Premature < 28 weeks
    - CNS depression by e.g. Anoxia, anesthesia or intra cranial hemorrhage
  - Reflex persisting beyond 6 months is seen in neurodevelopmental disorders e.g. cerebral palsy , autistic disorders

Grasp Reflex

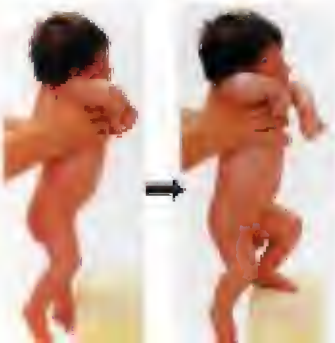
	Palmar grasp reflex	Solar grasp reflex
Present	From birth to 2 months	From birth to 10 months
Stimulus	 Light touch to the palm	 Light touch to the sole
Response	Grasp response	
Clinical value	• Normal reflex in the normal time frame →Normal newborn neurodevelopment • Help estimation of the gestational age; develops at 28 weeks and become fully mature by 32 weeks gestation • Absent in the same side of Klumpke's palsy	

Stepping Reflex

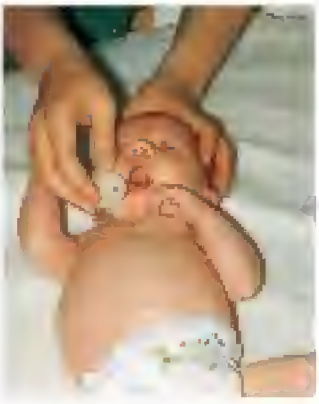
- Present at birth and disappear by 6th week of age
- Stimulus: Hold the baby upright with his soles touching a flat surface
- Response: the baby starts walking movements

Placing Reflex

- Presents at birth and disappears by 6th week of age
- Stimulus: Hold the infant upright with one foot touching a surface of table and the dorsum of other foot touching the under edge of the table
- Response: The baby will flex then extend the leg to place it on upper surface of the table



Rooting Reflex

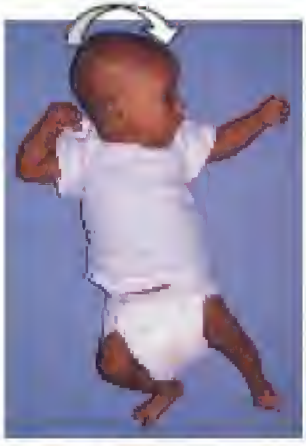


- Present at birth and disappear by the 4th month of age
- Stimulus: Stroke the baby's cheek
- Response: The baby will turn towards the stimulus and open his mouth, usually looking for food
- Retained reflex in older children is associated with poor articulation and messy eaters

Spinal Galant Reflex

- Present at birth and disappear by 3-9 months of age
- Stimulus: lay the baby on his stomach and stroke along one side of his spine.
- Response: The baby will flex sideways toward the stimulated side
- Retained reflex in older children is associated with inability to sit still ('ants in the pants' child), and possible scoliosis

Asymmetric Tonic Neck Reflex (ATNR)



- Appear by the 1st month and disappear by the 6th months of age
- Stimulus: While in supine ,Turn the baby's head to one side
- Response: The baby will extend the arm and leg on this side while his other arm and leg will flex (fencer position)
- Clinical Value
  - It prepares the baby for future movements like turning from back to front and vice versa
  - Infant "stuck" in the fencing posture, is always abnormal and implies a CNS disorder
  - Retained reflex in older children is associated with possible scoliosis, and poor handwriting in childhood

Landau Reflex

- Appear by the 3rd month and disappear by 24 months of age
- Stimulus: hold the baby in a prone (face down) position
- Response: The baby will extend head, trunk and limbs
- Clinical value:
  - A postural reflex that the infant needs to develop to sit and walk independently.
  - Absent in cerebral palsy

Parachute Reflex

- Present from 8-10 months and persist
- Stimulus: Hold the infant's trunk and then suddenly lower the infant as if he is falling.
- Response: The arms will spontaneously extend to brake the infant's fall, making
- Clinical value:
  - Protective reflex (a prerequisite to walking)

(Reference: Nelson Textbook 2016, Pediatric Neurology Seminars, 2010)

Incubator care for critically ill neonate /very low birth weight

General care

- Temperature: 29-36 °C ;depending on birth weight ; core temp :36.5-37 c
- Humidity : 60 - 80% ; reduce insensible water loss
- Minimal handling and strict anti septic measures

Support Respiration

- Supply oxygen as needed by:
  - Ambient oxygen
  - Head box
  - Nasal catheter/Vapotherm
- Assisted ventilation: CPAP, BiPAP
- Mechanical ventilation
- Monitoring: pulse oximeter, Blood gases

Support Circulation

- Vascular access
- Intravenous fluids
- Transfusions : packed RBCs, fresh frozen plasma, albumin
- Inotrpes e.g. Dopamine / dobutamine infusion
- Monitor :blood pressure, heart rate and capillary refill time

Support Nutrition

- Expressed breast milk or formula by nasogastric tube if enteral intake possible
- Total parenteral nutrition if enteral intake impossible(TPN consists of intravenous infusion of dextrose,amino acids , lipid, vitamins and minerals)

Specific treatment

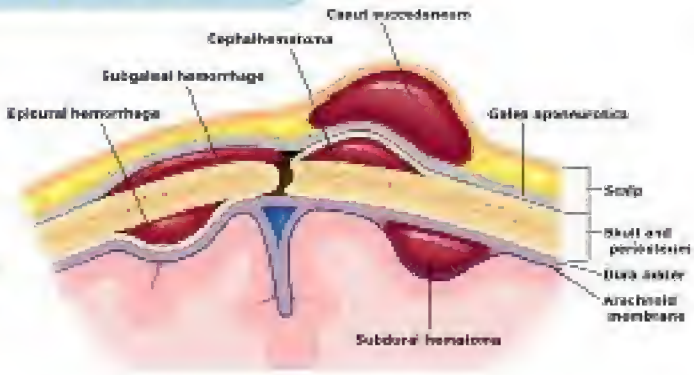
- Phototherapy for jaundice
- Antibiotics for sepsis
- Anticonvulsants for seizures

Monitoring

- Vital data
- Fluid balance: Daily hydration state , weight, urine output, serum sodium
- Bloods: Blood glucose, electrolytes, CBC, CRP, sepsis workup…
- Drug levels and TPN follow up lab

Birth Injuries

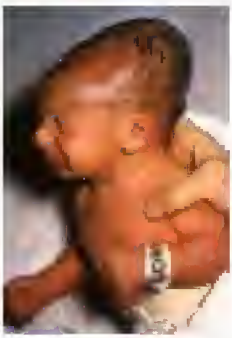
Cranial Injuries



1. Caput succedaneum

Subcutaneous fluid collection
Seen immediate after birth

Criteria



- Diffuse scalp swelling (cross the suture lines)
- Over the presenting part of the head
- Soft consistency
- May be with ecchymosis of the overlying skin

Treatment: Nothing required; it resolves in few days

2. Cephalhematoma

Sub-periosteal blood collection seen few hours after birth

Criteria

- Localized scalp swelling (never cross sutures lines)
- Over any bone (commonly parietal or occipital)
- Firm consistency
- Possible associations:
  - Linear fracture in 15-20%
  - Anemia and jaundice (if large)

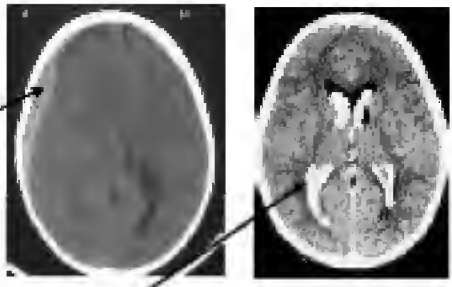
Treatment

- Observe ; most cephalhemaomas resolves spontaneously over 8 weeks
- Treat complications
  - Blood transfusion for anemia
  - Phototherapy for jaundice
  - Antibiotics, Incision and drainage for infection
- Avoid diagnostic aspiration→ carries risk of infection

3. Intracranial Hemorrhage (ICH)

Risk factors

- Birth trauma
- Bleeding disorder
- Perinatal asphyxia (esp. in premature)



Types

- Subdural hemorrhage
- Subarachnoid hemorrhage
- Germinal matrix hemorrhage / intraventricular hemorrhage (GMH/IVH):
  - Mainly in preterm; mainly in the first 3 days of life
  - Starts in the highly vascular periventricular germinal matrix then may extend to the ventricular system

Clinical picture

- Asymptomatic: Common; basically with GMH / IVH
- Mild hemorrhage
  - Reduced spontaneous movements
  - Hypotonia , poor suckling and Moro
  - Apneas
  - Anemia and fall of hematocrit
  - Abnormal eye movements
- Severe hemorrhage
  - Bulging fontanels
  - Decerebrate posturing
  - Hypotension, Collapse
  - Hypoxia
  - Seizures

Diagnosis

- Cranial CT scan or MRI
- Cranial ultrasonography:
  - Very sensitive & quick in diagnosing GMH/IVH
  - Infants <1,000 g are at highest risk and should undergo cranial ultrasonography within the 1st 3-7 days of age
- Coagulation profile (PT, PTT, platelets)
- CBC for anemia

Prevention of IVH

- A single course of antenatal steroids for 24-34 wk pregnancies of gestation that are at risk for preterm delivery
- Low-dose indomethacin (0.1 mg/kg/day for 3 days) to VLBW preterm infants reduces the incidence of severe IVH
- Avoid fluctuation in cerebral blood flow by regulating blood pressure and PaCO2
- Reduce infants fighting the ventilator by using synchronized ventilation and minimal handling and minimal ETT suctioning
- Correct any coagulopathy

Treatment

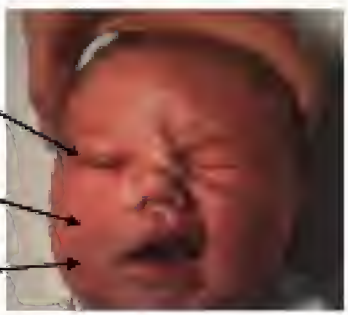
- Supportive care in NICU
- Treat anemia with blood transfusion
- Correct any coagulopathy
- Consider starting inotropes e.g. Dopamine if hypotension persists
- Symptomatic treatment for e.g. seizures, raised intracranial tension
- Repeat cranial ultrasound at intervals (usually within 3-5 days then weekly)
- Neuro Surgical consultation

Nerve Injuries

1. Facial nerve injury

Peripheral facial nerve injury results in paralysis of whole face on the same side:

- Inability to close the eye firmly
- Absent nasolabial fold.
- Asymmetric cry.
- Deviation of the mouth to healthy side



Treatment

- Care of the eyes with → eye drops & ointment.
- Care of feeding
- Physiotherapy → if persist more than 3 months → neuroplasty

2. Brachial plexus injury

a. Duchenne-Erb's palsy

- Injury to the upper nerve roots (C_5, C_6) of brachial plexus
- Paralysis of upper arm muscles with loss of abduction, external rotation and supination

Criteria

Look: The arm is adducted, internally rotated and pronated (*Waiter's tip posture*)

Test: Lost Moro reflex, and preserved Grasp reflex on the affected side

Association: Phernic nerve palsy in 75 % of cases

- Present with respiratory distress, and predominant thoracic breathing
- Diagnosed by :chest x ray (inspiration film) and fluoroscopy (detect paradoxical movement)

Treatment

- Partial intermittent immobilization in opposite position i.e. abduction, external rotation and supination (*Statue of liberty splint*)
- Physiotherapy after one week (after resolution of nerve edema) to prevent muscles contractures

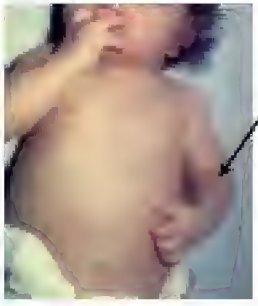
Prognosis

- Full recovery occur in more than 90% by 3 months
- If no improvement within 3 months, consult neurosurgery

b. Klumpke's palsy

- Injury to the lower nerve roots (C_7, C_8, T_1) of brachial plexus
- Paralysis of all intrinsic muscles of the hand

Criteria



Look: Claw-hand deformity

Test : Lost Grasp reflex, and preserved Moro reflex on the affected side

Association: Horner syndrome if sympathetic fibers of T_1 are involved → ptosis, meiosis, enophthaloms and anhydrosis

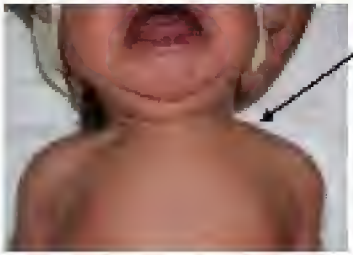
Treatment

- Hand is kept in neutral position with pad of cotton in the fist (*hand writing position*)
- Physiotherapy

Bone Injuries

Fracture clavicle

Commonest bone to be fractured in neonates especially if large and breech



Look:

- Bone irregularity and Crepitus on the affected side
- Pseudo paralysis of the affected limb
- May be excessively irritable newborn

Test: Moro reflex → Absent Moro on the affected side

Request: Chest X ray→diagnostic (soft tissue ultrasound has equal sensitivity and safer)

Treatment

Immobilization of arm and shoulder (figure 8 bandage)

Soft tissue Injuries

1. Liver or Spleen

Clinical picture

- Severe pallor → up to hypovolemic shock .
- Indirect hyperbilirubinemia
- Abdominal distension with discoloration of abdominal wall.
- Abdominal ultrasound is diagnostic.(? paracentesis)

Treatment

- Blood transfusion.
- Surgical exploration

2. Adrenal hemorrhage

Risk factors

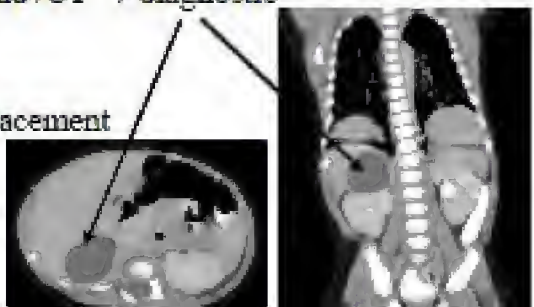
- Neonate adrenals are large, friable, highly vascular .
- Unilateral in 90%; mainly on the right side.

Clinical picture

- Pallor
- Flank mass
- Adrenal insufficiency: vomiting , poor feeding , shock .
- Abdominal ultrasound /CT → diagnostic

Treatment

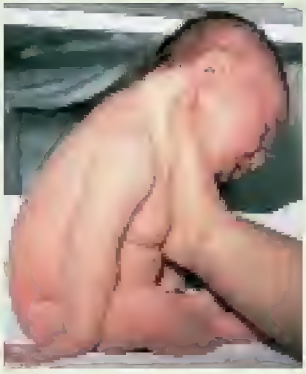
- Blood transfusion
- Intravenous fluids
- Corticosteroids replacement



Self assessment case scenarios

Case 3

This newborn infant develops tachypnea with cyanosis. She improves somewhat on oxygen but has predominantly thoracic breathing movements, and the chest x-ray, which appears to have been taken inadvertently at expiration, seems normal.



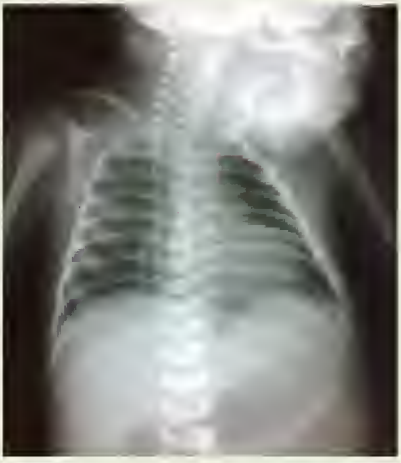
A. The procedure most likely to provide a specific etiologic diagnosis is

1. Venous blood gas
2. CT scan of the head
3. Fluoroscopy of the chest
4. Bronchoalveolar lavage
5. Blood culture

B. What is the diagnosis?

Case 4

You are asked to review a baby on the postnatal wards 12 hours of age after a difficult breech delivery.
The baby was said to be fractious and is not feeding.
As a part of sepsis screen chest X ray was carried out
What is the diagnosis?



Case 5

A term 3.5 kg female baby at 34 hour of life was admitted for unexplained pallor and abdominal distension, she was born to 29 years old mother by difficult breech vaginal delivery and she had poor Apgar score at birth. On examination she was very pale ,jaundiced ,tachycardic and tachypneic. Abdominal examination revealed a smooth non tender mass in the right flank with no evidence of free fluid. Hb% was 6.8gm/dl ,indirect bilirubin 14 mg/dl, PT >30 seconds, PTT >60 seconds .Urea, creatinine and liver enzymes were normal

a. **What is the expected diagnosis?**
b. **What is the investigation of choice?**
c. **What are the 4 main initial lines of treatment?**

Neonatal Septicemia

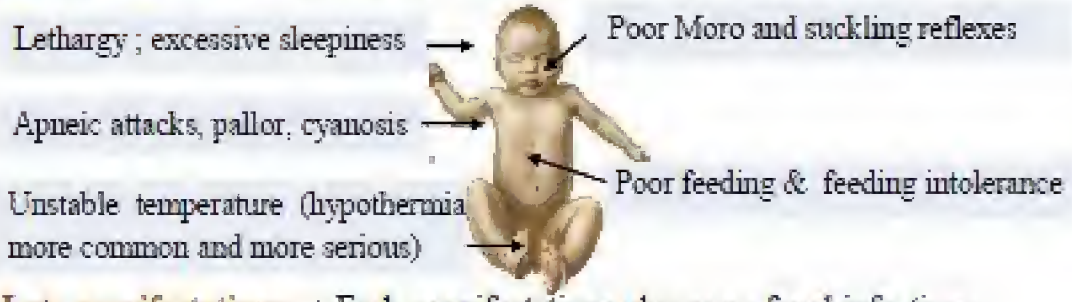
Definition: Serious systemic infection of the newborn.

Classification

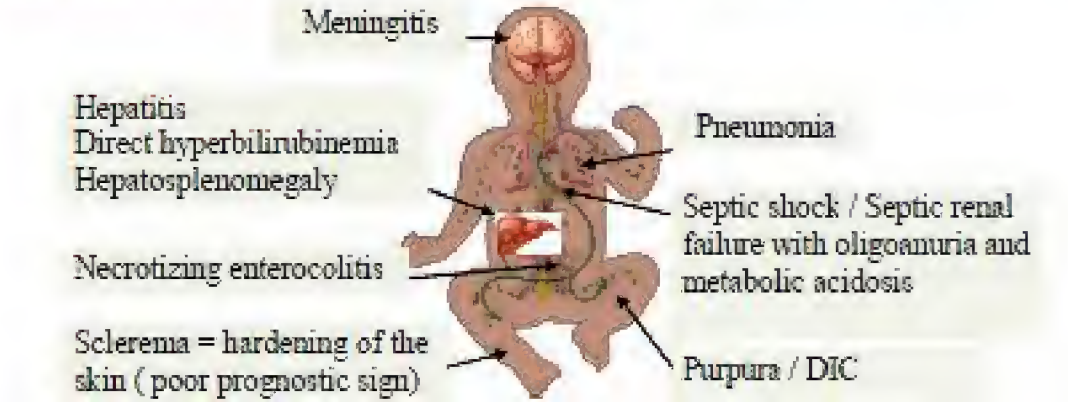
	Early sepsis	Late and nosocomial sepsis
Pattern	Acquired before or during delivery (vertical mother-to-child transmission)	Develop after delivery from organisms acquired in the hospital or the community
Onset	In the 1st week (usually <72 hr)	After the 1st week
Risk factors	• Prematurity • Premature rupture of membranes > 18 hr. • Chorioamnionitis • Maternal intrapartum fever ≥38.0°C • Maternal bacteruria.	• Prematurity. • Hospitalization • Umbilical catheterization , or poor cord care • Endotracheal intubation • Mechanical ventilation.
Organisms	• Group B streptococci (GBS) • E.Coli • Listeria monocytogenes	• Staphylococcus Aureus. • Hemophilus influenza • Klebsiella. • Pseudomonas. • Viral or candida

Clinical picture

1. Early manifestations ⇒ Non specific = Not doing well baby



2. Late manifestations ⇒ Early manifestations plus more focal infections



3. **Presence**: of one or more risk factors especially in premature or mechanically ventilated baby with persistent metabolic acidosis should suspect sepsis until prove otherwise. (Antibiotics must be used till negative cultures are obtained).

Diagnosis

1. **History** : for risk factors
2. **Clinical picture**
3. **Investigations**
   a. **Sepsis screen**: Septicemia is suggested when:
      CBC findings
      - Leucopenia < 5000/mm^3 (with severe sepsis)
      - Toxic granulations in neutrophils.
      - Bandemia: Band cells (immature) >20% of total neutrophil count.
      - Less commonly leucocytosis (> 30.000 / mm^3)
      - Thrombocytopenia

      Markers of inflammation
      - Serial determination of C-reactive protein (CRP)
      - ESR

   b. **Detect causative organism by**
      - Cultures of Blood, CSF, urine, and endotracheal aspirate.

   c. **Evidence of Multiorgan System Disease**
      1- Pulmonary: Chest x ray for pneumonia, blood gases
      2- CSF analysis, culture and gram stain for meningitis
      3- Liver enzymes, bilirubin, ammonia, prothrombin time, PTT
      4- Serum urea and electrolytes, blood glucose

Differential diagnosis

Other causes of critically ill neonate: THE MIS FITS

T : Trauma e.g. intracranial hemorrhage
H : Heart disease e.g. congenital ,hypoxic, hypovolemic
E : Endocrine e.g. congenital adrenal hyperplasia
M : Metabolic disturbances e.g. hypoglycemia , hypocalcemia
I : Inborn errors of metabolism
S : Sepsis
F : Fits(seizures)
I : Intestinal catastrophes e.g. intestinal obstruction, NEC
T : Toxins
S : Severe asphyxia

Management

A. Prophylaxis

Maternal intrapartum ampicillin prevent perinatal transmission of GBS

Indications

- Previous infant with invasive GBS disease
- GBS bacteruria during current pregnancy
- Positive GBS screening culture during current pregnancy (unless a cesarean delivery is performed before onset of labor or amniotic membrane rupture)
- Unknown GBS status at the onset of labor and any of the following:
  - Delivery at <37 weeks' gestation
  - Amniotic membrane ruptue ≥18 hr
  - Intrapartum temperature ≥38.0°C

B. Curative

1. Incubator care in neonatal intensive care unit (NICU)

(See before)

2. Specific treatment

- Immediate parenteral antibiotics are initiated after taking appropriate cultures.
- Antibiotics are given according to culture and sensitivity(C/S)
- While waiting for C/S ; empiric antibiotic combinations is given:
  - For early onset sepsis: Ampicillin plus Gentamicin
  - For late onset sepsis: Vancomycin(or oxacillin) plus Gentamicin
  - Some experts recommend antifungal prophylaxis with fluconazole for particularly high-risk newborns—that is, those of extremely LBW (<1000 g) and low gestational age (<27 wk).
  - Third-generation cephalosporins such as cefotaxime or ceftazidime are valuable additions for treating documented neonatal sepsis and meningitis
  - All antibiotics should be given for **10-14 days (3weeks for meningitis).**
  - Dose and interval of antibiotics depends on birth weight and gestational age
  - Peak and trough levels of Gentamicin and Vancomycin are useful to ensure therapeutic levels and minimize toxicity

3. Treatment of complications

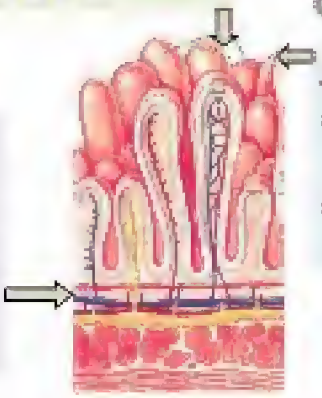
Necrotizing Enterocolitis (NEC)

Definition

Syndrome of acute intestinal necrosis of unknown cause usually affects sick prematures with high mortality rate.

Risk factors

1. **Prematurity**
   - The most important risk factor
   - NEC affects 10% of infants < 1500 gm

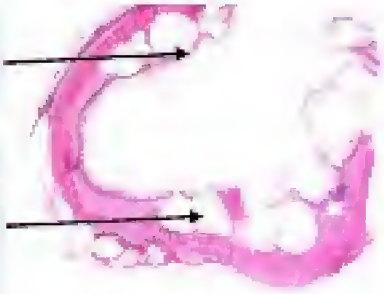


2. **Intestinal ischaemia** due to
   - Perinatal asphyxia
   - Patent ductus arteriosus and indomethacin
   - Polycythaemia
   - Umbilical catheterization

3. **Feeding**
   - Non breast feeding with hyperosmolar formula
   - Aggressive enteral feeding in prematures

Pathogenesis

- Sloughing and necrosis of the intestinal mucosa especially at terminal ileum and proximal colon



- Superadded infection (Klebsiella, E-coli, Clostridia, & Viruses) ⇒ Gas formation within the bowel wall → extensive bowel necrosis and Septicemia → perforation & peritonitis

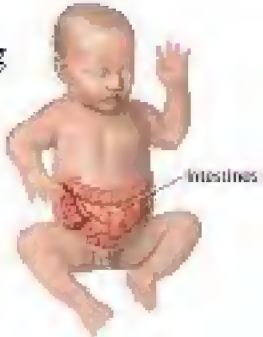
- Platelet activating factor, tumor necrosis factor and cytokines may play role

Clinical picture

Presentation is usually within 1st 2 weeks of life

A. **Nonspecific Systemic signs**: any combination of the following

- Apnea
- Lethargy
- Decreased peripheral perfusion
- Shock (in advanced stages)
- Cardiovascular collapse
- Bleeding diathesis (consumption coagulopathy)



B. Abdominal manifestations

- Feeding intolerance
- Delayed gastric emptying
- Abdominal distention (↑abdominal girth)
- Abdominal tenderness
- Ileus/decreased bowel sounds
- Abdominal wall erythema (advanced stages)
- Hematochezia

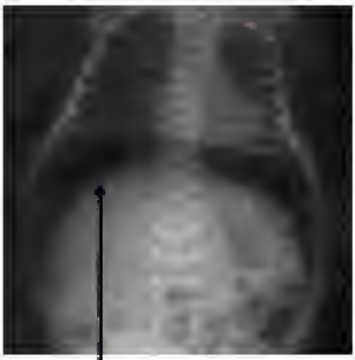
Investigations

A. Radiological

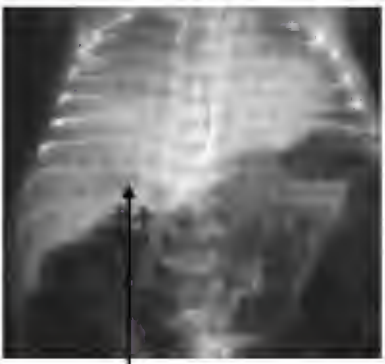
1. X-ray abdomen

- View: Antero posterior and lateral
- Should be done and repeated every 8 hours in the first 2 days
- Findings

Pneumatosis-intestinalis (gas in the intestinal wall)



Pneumo-peritoneum (gas under the diaphragm) if perforation occurred



Intrahepatic portal venous gas

2. Abdominal ultrasound

- Sensitive for pneumatosis-intestinalis but require skilled sonographer
- Doppler of the splanchnic arteries can distinguish very early NEC from benign feeding intolerance in a mildly symptomatic baby

B. Laboratory findings

- Triad of thrombocytopenia, hyponatremia and metabolic acidosis.
- Stool examination for occult blood (Gauiac test).
- Sepsis workup: CBC, CRP and Culture of blood, stool, and CSF

Prevention

- Breast milk reduce the incidence of NEC.
- Avoid aggressive feeding in preterm
- Prenatal corticosteriods

Treatment

Admit	○ To NICU for full monitoring and supportive care
Stop	• Enteral feedings for 7-14 days according to severity
Start	○ GIT rest and nasogastric deconpression
	○ Intravenous fluids / Total Parenteral Nutrition (TPN)
	○ Broad-spectrum antibiotics ; Ampicillin /Gentamicin /and either Clindamycin or Metronidazole)
Support	• For respiratory failure (oxygen therapy, ventilation)
	• For cardiovascular failure(fluid resuscitation, pressors)
Consult	○ Pediatric surgeon at the earliest suspicion of developing NEC

Congenital Infections (TORCH)

Etiology

Toxoplasmosis	Congenital Rubella	Cytomegalovirus	Herpes simplex type II
Toxoplasma gondii protozoan inhabit cats' gut → oocytes in their stool → contaminate food, water & in raw meat of infected cattles	Maternal german measles specially in the 1st trimester	DNA virus infection can be: ○ Transplacental ○ Perinatal ○ In breast milk	DNA virus infection can be : ○ Transplacental ○ Contact with genital lesions during vaginal delivery→ common

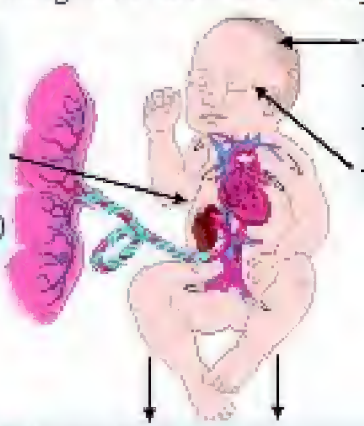
General clinical features

A. History suggestive of congenital infection

- Previous abortions or intra uterine fetal death
- Maternal Fever ,Skin rash or Skin vesicles during pregnancy

B. General features suggesting congenital infection : may be

- ○ Hepatosplenomegaly
- ○ Generalized lymphadenopathy.
- ○ Anemia
- ○ Thrombocytopenic purpura.
- ○ Hepatitis (↑conjugated bilirubin)



- Mental retardation
- Seizures
- Microcephaly
- Chorioretinitis

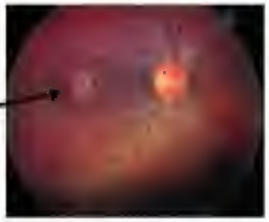
Low birth weight

- Intra uterine growth restriction
- Prematurity

General workup

- Detection of specific IgM or rising titer of specific IgG
- For clinical features e.g.
  - CBC with differential WBCs count
  - Fundus examination
  - Liver enzymes and bilirubin
  - Plain skull radiograph, CT, MRI
- Isolation of the causative organism

Congenital Toxoplasmosis

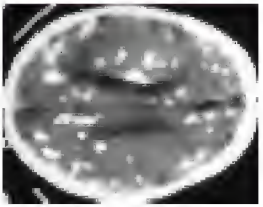


Clinical picture

- General features
- Hydrocephalus /Microphthalmia /Chorioretinitis

Diagnosis

- General workup
- Isolate of the organism from the blood
- Skull X-ray, CT: Diffuse calcifications



Treatment

A. Prevention

- Food hygiene
- Spiramycin for seropositive pregnant

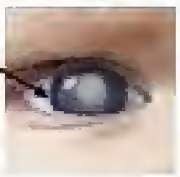
B. Curative

- Symptomatic treatment
- Triple therapy for up to 1 year pyrimethamine ,folonic acid, sulphadiazine

Congenital Rubella Syndrome(CRS)

Clinical picture

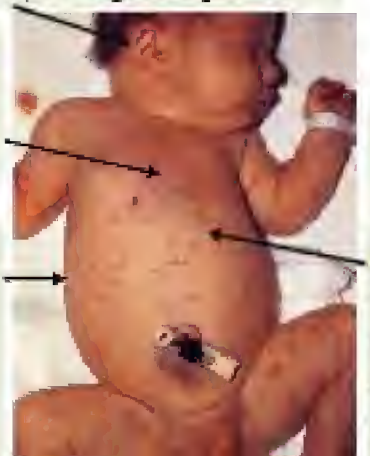
- Even if asymptomatic infection occurs in the mother, rubella can be transmitted across the placenta to the developing fetus.
- The earlier in gestation the infection occurs, the greater the injury
- 40% of fetuses infected during the first 8 weeks spontaneously abort
- Some infants at risk are normal
- Some appear normal at birth but later are found to have hearing loss
- Some are small for gestational age and at birth have congenital anomalies :
  - Cataract, glaucoma, microphthalmia
  - Sensorineural deafness , Miningeoencephalitis



Chorioretinitis
(salt and pepper appearance)

Congenital heart disease

- PDA
- Pulmonary stenosis



- Hepatosplenomegaly
- Lymphadenopathy
- Anemia
- Purpura
- Hepatitis

In some cases a rubelliform rash or a characteristic raised, bluish, papular eruption, termed a blueberry muffin rash, may be evident as the result of dermal erythropoiesis

Prognosis

Survivors of rubella syndrome are highly likely to be deaf and have significant psychomotor retardation

Diagnosis

- General workup
- Viral culture and specific IgM titers

Treatment

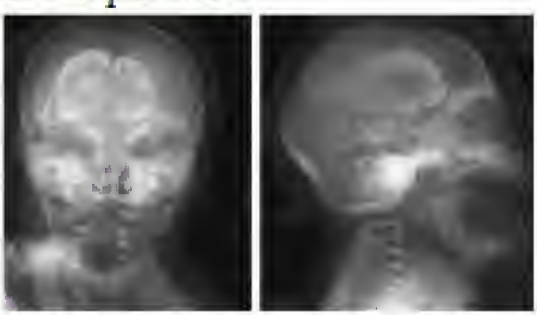
- Infants with congenital rubella are chronically infected and tend to shed live virus in urine, stools, and respiratory secretions for up to a year. Hence, they should be isolated when in the hospital and kept away from susceptible pregnant women when sent home
- Symptomatic treatment

Prevention

- Rubella or MMR vaccine
- Pregnant exposed to German measles→ abortion or I.V Immunoglobulin

Congenital CMV Infection

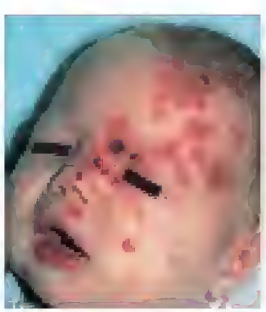
- General clinical features and general workup as before
- Isolate the virus from urine
- Periventricular calcifications



Treatment

- Hyperimmune anti-CMV immunoglobulin.
- Symptomatic treatment
- Ganciclovir
- Avoided by blood products screening

Congenital HSV Infection



- Skin and mouth vesicles and ulcers
- Kerato conjunctivitis
- Encephalitis
- Disseminated form: (multi organ) ⇒ septic shock like

Diagnosis

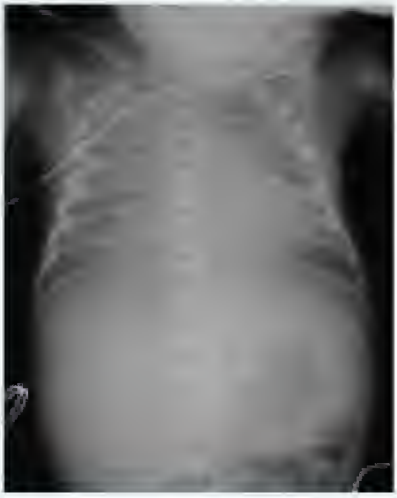
- Isolate CMV from the vesicles or conjunctiva smears
- Skull X-ray, CT: May show diffuse calcifications
- Avoided by cesarean section for mothers with genital lesions and Acyclovir

Treatment: Symptomatic treatment ÷ Acyclovir or Vidarabine

Self-assessment case scenarios

Case 6

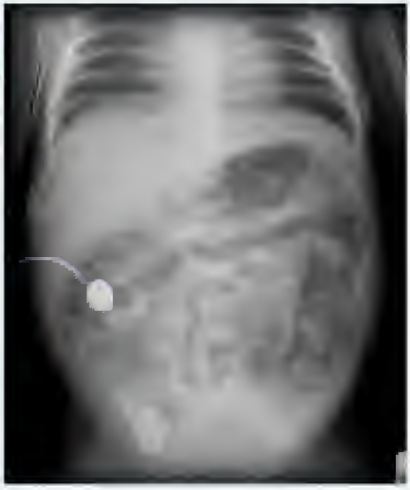
This is a 3.2 kg term newborn female delivered via normal spontaneous vaginal delivery. Rupture of membranes occurred 21 hours prior to delivery with clear fluid. There was a maternal fever 38.1C. Apgar scores were 8 and 9. The infant appears slightly pale and mottled, with persistent grunting, shallow respirations, and lethargy Her fontanels and Heart exam were normal.
Chest x ray is shown



a. **What is the likely diagnosis?**
b. **Comment on the X ary ?**
c. **What are further investigations required ?**

Case 7

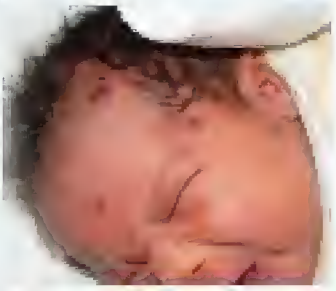
A 28 weeks gestation infant has been born and has needed relatively little ventilator support. Feeds are introduced on day 3 and increased slowly. on day 5 he deteriorates and there was obvious abdominal distension. An abdominal X ray is obtained



a. **What does the x ray show?**
b. **What do you think has happened?**
c. **What will you do next?**

Case 8

A baby boy delivered at 38 weeks' gestation with a birth weight of 2 kg and a head circumference of 31 cm . At day 3 postnatal , he had neonatal thrombocytopenia requiring platelet transfusion. Later, brainstem evoked responses indicated severe bilateral sensorineural deafness. His mother had a contact at 9 weeks' gestation with a family member with rash, and she developed same illness 1 week later.



a. **What is the diagnosis?**
b. **What is the skin lesion seen?**

Neonatal Jaundice

- Jaundice: is yellowish discoloration of skin and mucus membranes due to increased serum bilirubin above normal levels
- Normal cord bilirubin is less than 3 mg/dl.
- Jaundice is obvious clinically in neonate when serum bilirubin exceeds 5 mg/dl

Bilirubin Metabolism

1. Production: Bilirubin is produced mainly from old RBCs

- Old RBCs give rise to globin and haem
- Globin enter the amino acid pool of the body
- Haem spilt into iron and biliverdin which change into unconjugated bilirubin
- Unconjugated (indirect) bilirubin has 3 criteria:
  - Fat soluble→ can cross Blood Brain Barrier (BBB)
  - Water insoluble → can not be excreted in urine
  - Detected by indirect Van Den Berg reaction

2. Transport

Indirect bilirubin is carried on albumin (unconjugated or hemebilirubin)

3. Uptake by hepatocytes

Bilirubin bind to cytoplasmic ligandins ; Z & Y proteins to deliver it to endoplasmic reticulum where conjugation occur.

4. Conjugation

Conjugation of bilirubin stimulated by glucoronyl transferase enzyme give rise to conjugated or cholebilirubin which is water soluble (excrectable in urine) and lipid insoluble (cannot cross BBB)

5. Secretion

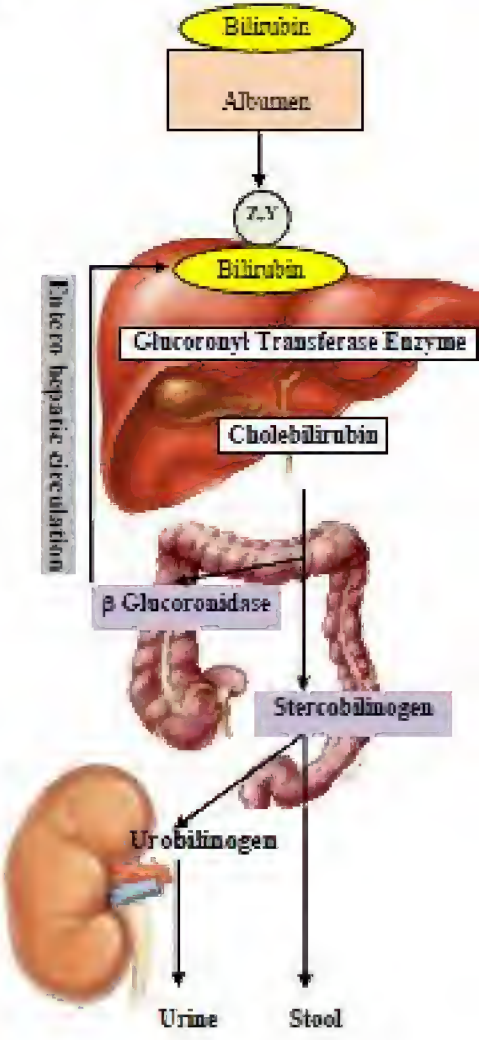
Active secretion of conjugated bilirubin by liver cells into bile canaliculi.

6. Excretion

Excretion of conjugated bilirubin & bile salts into the intestine.

7. Bilirubin in intestine

- Some amount is deconjugated by mucosal enzyme; β glucoronidase → unconjugated bilirubin → reabsorbed to the liver (entero- hepatic circulation)
- Some amount is changed to stercobilinogen → stool
- Small amount of stercobilinogen reach the systemic blood (urobilinogen) → urine.



Unconjugated Hyperbilirubinemia

High Total Serum Bilirubin (TSB) & conjugated bilirubin < 15 % of TSB

Causes

1. **Bilirubin over production**

I. Increased rate of hemolysis (Reticulocyte count elevated).

a- Direct Coomb's test positive
- Rh. incompatibility.
- ABO blood group incompatibility

b- Direct Coomb's test negative
- Spherocytosis
- α Thalassemia
- Glucose-6-phosphate dehydrogenase deficiency.

II. Non hemolytic causes (normal reticulocyte count.)

- Extra vascular hemorrhage : Cephalhematoma & Internal hemorrhage
- Elevated RBCs load (Polycythemia) → ↑ RBCs turnover
- Enhanced enterohepatic circulation of bilirubin 2ºº to gastro intestinal stasis e.g. congenital pyloric stenosis and breast feeding jaundice

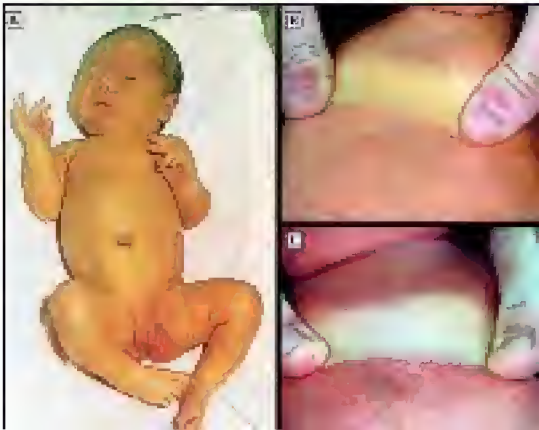
2. **Defective uptake**: Due to defective ligandins (Z&Y proteins)

3. **Defective conjugation**: Glucoronyle transferase enzyme may be:

- Absent → Criggler – Najjar syndrome type I
- Deficient → Criggler – Najjar syndrome type II
  → Gilbert syndrome
- Immature → Physiologic jaundice
- Under stimulated → Hypothyroidism, hypoglycemia, hypoxia
- Inhibited → Breast milk jaundice, Lucy- Driscoll syndrome

Clinical features

- Skin and sclera: bright yellow / orange
- Color of urine: usually normal.
- Color of stool : may be dark
- Possible Concurrent problems:
  (Absent in physiologic jaundice)
  * Risk of kernicterus if indirect bilirubin exceeds the binding sites on albumin or with leaky blood brain barrier
  * Risk of anemia: if hemolysis exists



- Timing of Clinical jaundice:

* In the 1st day of life	- Hemolytic disease of newborn (Rh or ABO incompatibility *(until prove otherwise)*.
* In the 2nd - 3rd day of life	- Physiologic jaundice - Criggler Najjar syndrome - Hemolytic anemia
* By the 4th –7th days	- Physiologic jaundice in premature - Hemolytic anemia
* After the 1st week	- Breast milk jaundice - Hemolytic anemia
* Persistent > 3rd week	- Criggler-Najjar syndrome - Physiologic jaundice in hypothyroid infant

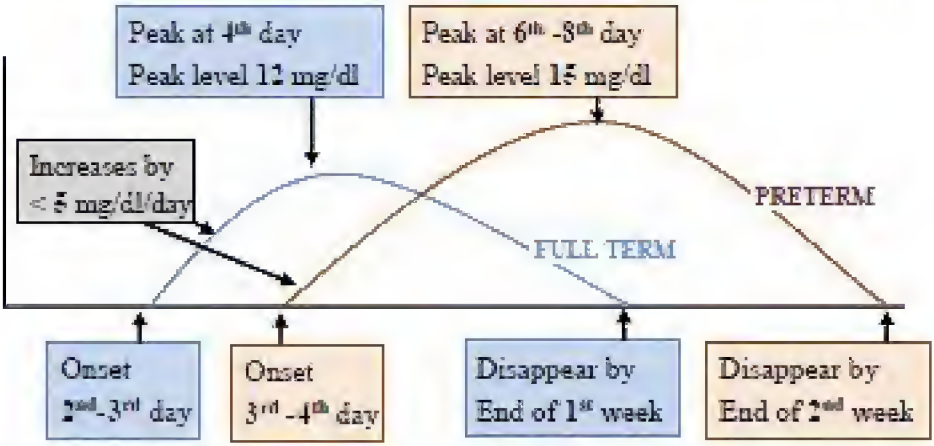
Physiologic Jaundice

Incidence - Affects 40-50% of full term and 60% of preterm

Etiology
- Transient glucuronyl transferase enzyme immaturity .
- Metabolism of extra hemoglobin formed intrauterine
- Shorter life span of neonatal RBC's
- Reduced Z & Y proteins (Ligandins) during the 1st week

Characters

- Unconjugated hyperbilirubinemia (Direct bilirubin <1mg/dl)



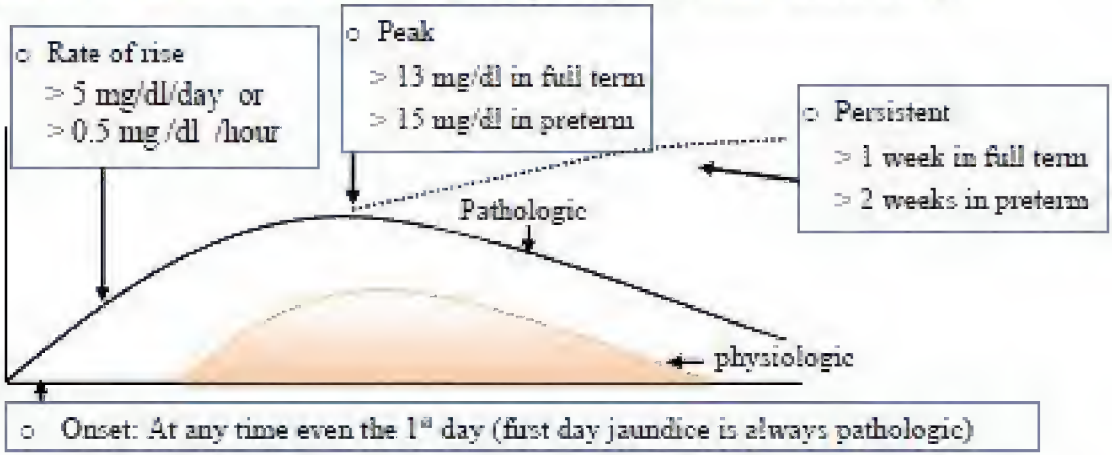
- No pallor, organomegaly nor risk of kernicterus
- Diagnosed by exclusion (Well baby, No hemolysis, nor anemia)

Treatment - Usually need no treatment; especially in full term
- Phototherapy or even exchange may be needed for VLBW

Differential diagnosis: From pathological jaundice

Criteria of pathological jaundice

Jaundice is considered pathologic if the time of appearance, duration, or pattern varies significantly from physiologic jaundice or if the course is compatible with physiologic jaundice but the infant has other risk factors predisposing him to neurotoxicity :



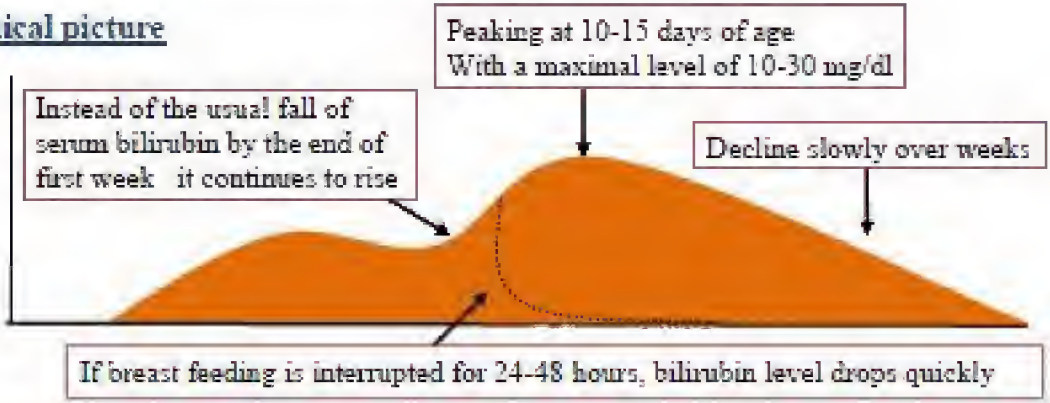
- Associated problems (e.g. anemia, organomegaly, signs of sepsis, kernicterus).
- Non response to phototherapy
- Direct hyperbilirubinemia is always pathologic.

Breast Milk Jaundice

Incidence

- Affects 2-4 % of adequately breast fed, healthy full term.
- Recurrence rate 70% in subsequent pregnancies

Clinical picture



Etiology Unknown ; Breast milk may contain:

- Pregnandiole → inhibit glucoronyle transferase enzyme.
- β glucoronidase → enhance entero hepatic circulation of bilirubin

Diagnosis - By Exclusion (Normal liver functions &CBC) + Therapeutic trial

Gilbert Disease

Etiology
- Autosomal dominant disorder.
- Decreased hepatic glucoronyle transferase level.(was thought to be due to deficiency of Z& Y proteins)

Clinical picture
- Mild hyperbilirubinemia ,usually need no treatment

Criggler-Najjar Syndrome Type I

Etiology
- Autosomal recessive disorder.
- Absent glucoronyle-transferase enzyme

Clinical picture
- Severe disease; very high level of indirect bilirubin
- Unresponsive to phenobarbitone

Diagnosis
- Clinical picture
- Enzyme assay in liver biopsy

Criggler-Najjar Syndrome Type II

Etiology
- Autosomal dominant disorder.
- Partial deficiency of glucoronyl-transferase enzyme

Clinical picture
- Less severe than type I
- Responsive to phenobarbitone trial

Investigations of indirect hyperbilirubinemia

1- Total Serum Bilirubin (TSB) & direct fraction (direct fraction < 15 % of total)

2- Direct Coomb's test:
- If positive → check blood group of infant & mother.

3- Hb/Htc value:
- If high (Htc > 65%) → polycythemia.
- If normal or low (Hb <13gm/dl) → check Retics count

4- Reticulocyte count:
- Normal → extravascular hemorrhage.
- High (> 6%) → Check blood smear & osmotic fragility
  → G6PD enzyme assay.

5- Others
- Check albumin if TSB is approaching the exchange level
- Serum T_4 & TSH to rule out hypothyroidism if jaundice is prolonged
- Phenobarbitone trial for Criggler-Najjar type II.

6- For a risk factor:
- Sepsis screen If history and/or presentation suggest sepsis
- Cranial ultrasound /CT for cephalhematoma

Hb = hemoglobin ,Htc = hematocrit value, retics = reticulacytic count

Treatment of indirect hyperbilirubinemia

Goal of therapy:

- Prevent neurotoxicity related to indirect-reacting bilirubin regardless of the cause
- Keep the maximal total serum bilirubin below pathologic levels by phototherapy and, if it is unsuccessful, by exchange transfusion

1. Phototherapy

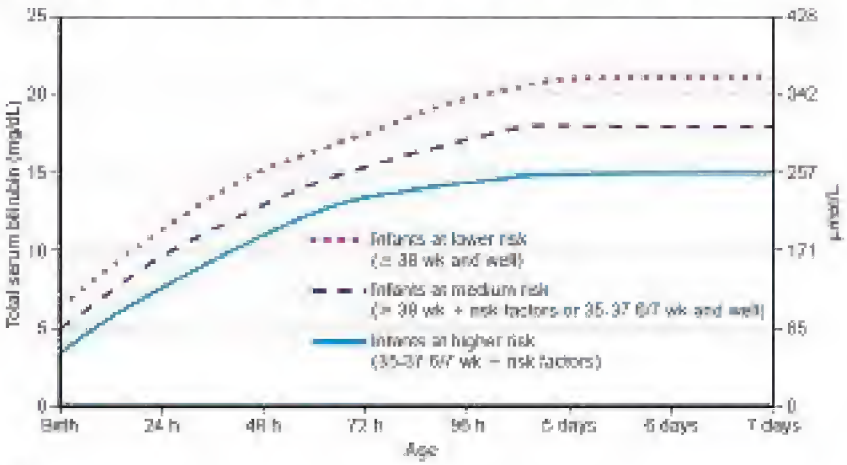
Idea

Exposure to blue-green spectrum (wavelengths 430–490 nm) → photo oxidises and isomerizes bilirubin → convert insoluble unconguated bilirubin to non toxic, soluble forms →↑ excretion via urine and bile

Indications

1. Treat moderately severe indirect hyperbilirubinemia in order to reduce need for exchange transfusion (In healthy full term at TSB 15-25 mg/dl and at lower levels in preterm and neonate with risk factors for kernicterus)
2. During waiting for exchange transfusion.

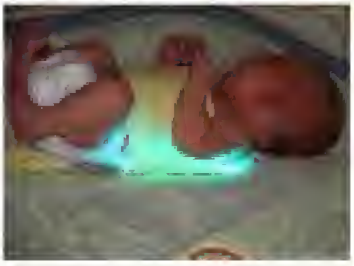
There is no consensus regarding exact bilirubin level at which to initiate phototherapy, so, Protocols using bilirubin nomogram , physical examination, and risk factors for kernicterus help decide the appropriate modality



Procedure

- Baby is completely naked except eyes and genitalia
- Change position every now and then
- Continuous exposure with short intervals for feeding
- Monitor temperature and hydration state frequently
- Monitor TSB every 4-24 hours according to infant's age ,condition and TSB level
- Discontinue when TSB fall 1.5-3 mg/dL below the level triggered the initiation of phototherapy

- Fiber optic blankets (Bili blankets) are recently used for home or hospital phototherapy in prolonged cases
- Follow up TSB 6-12 hr after cessation of phototherapy



Side effects

1. Loose stool
2. Skin rash and erythema of skin
3. Hyperthermia
4. Dehydration due to insensible water loss
5. Damage to exposed eye or genitalia
6. If used in direct hyperbilirubinemia → Bronzed baby syndrome

2. Exchange transfusion

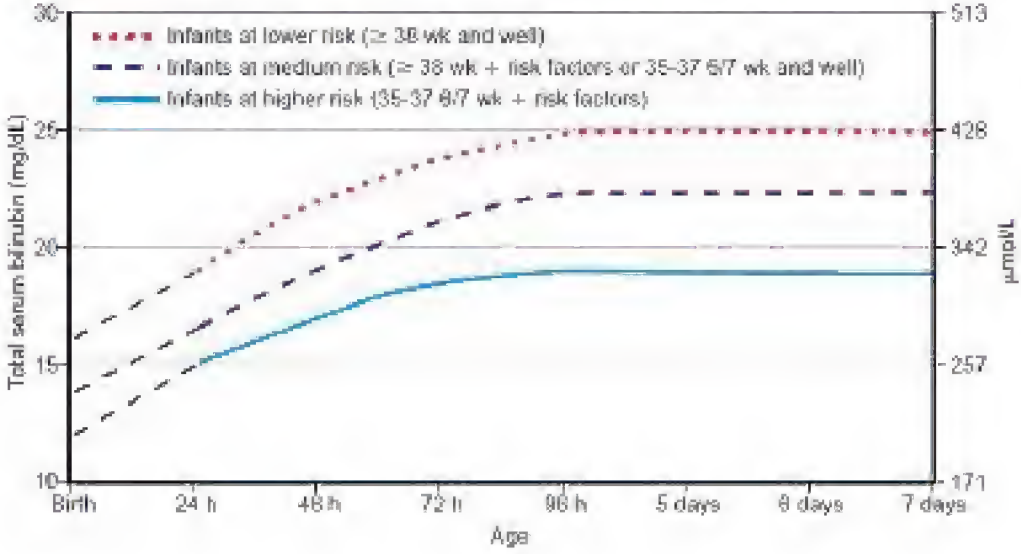
Indications

1- In Rh and ABO incompatibility

- Cord bilirubin > 5 mg/dl(normally <3 mg/dl)
- Cord hemoglobin < 10 gm/dl
- Rapid rise of bilirubin (> 1 mg/dl/hour) despite phototherapy
- Early signs of kernicterus
- Previous baby with kernicterus or severe erythroblastosis fetalis

2- In other causes: with high bilirubin level & phototherapy ineffective

- Healthy full term TSB→ ≥ 25 mg/dL
- Preterm and neonate with risk factors for kernicterus → at lower levels (reference tables & bilirubin nomograms also exist)



Idea

- Remove excess unconjugated lipid soluble bilirubin.
- Remove antibodies from the circulation

Procedure

- Extensive phototherapy while preparing for the exchange
- Blood used is:
  - Fresh, warm O negative blood
  - Compatible with both maternal and neonatal blood
- Amount = double the neonate blood volume (2×85 ml/kg).
- Small amounts (10-20 ml) are removed and replaced by equal amounts of the new blood through umbilical vein catheter
- Potential complications include apnea and bradycardia in preterm infants, hypocalcemia, thrombocytopenia, metabolic acidosis, and vascular spasm

3. Special Cases

a. Treat risk factors for kernicterus e.g.

- Antibiotics for septicemia
- Correction of acidosis
- Avoid drugs which displace bilirubin from albumin

b. Breast milk jaundice

- Stop breast feeding for 24 - 48 hours → Bilirubin fall quickly

c. Isoimmune hemolytic disease

- Intravenous Immunoglobulin 0.5-1.0 g/kg/dose; repeat in 12 hr
- Reduce need for exchange transfusion in both ABO and Rh hemolytic disease

d. Criggler Najjar Syndrome type II

- Phenobarbitone 5 mg/kg/d oral.
- Role: Stimulates glucoronyl transferase enzyme(enzyme inducer).
- Side effect: sedation → poor feeding

e. Criggler Najjar Syndrome type I

1- Repeated exchange transfusion & phototherapy

2- Oral agar → block enterohepatic circulation of bilirubin.

3- Metalloporphyrin → block heme oxygenase.

4- Hepatic transplantation

Kernicterus

(Bilirubin Encephalopathy)

Definition

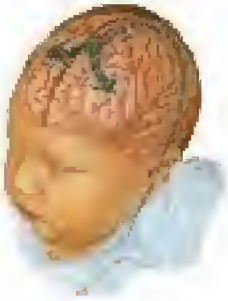
Yellowish staining of the cerebellar & cerebral nuclei (especially basal ganglia) due to deposition of unconjugated bilirubin resulting in neuronal necrosis.

Etiology

A. Level of serum unconjugated bilirubin exceeding critical values
- -> 10 mg/dl in the 1st day
- -> 15 mg/dl in the 2nd day
- -> 25 mg/dl afterwards

However kernicterus may occur at a lower levels in presence of risk factors:

a. Increased blood brain barrier permeability
- Prematurity & very low birth weight
- Acidosis
- Sepsis
- Asphyxia
- Anemia (Iso immune hemolysis ,G6PD ↓)



b. Defective albumin/ bilirubin binding
- Hypoalbuminemia < 3 gm /dl
- Hypothermia

B. Duration of exposure to the high bilirubin level:

The longer the duration the more risk of kernicterus.

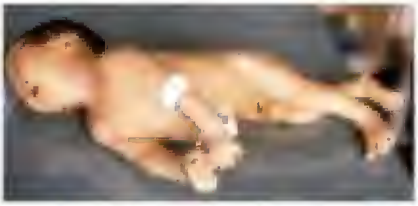
Clinical picture

Usually appear 2-5 days after birth in term infants and by the 7th day in preterm

A. Acute bilirubin encephalopathy

Early signs
- Lethargy, poor feeding and Lost Moro reflex are common initial signs
- High pitched cry and hypotonia with diminished tendon reflexes
- Respiratory distress
- Seizures

Few days later
- Hypertonia of extensor muscles
- Opisthotonos with a bulging fontanel
- Fever

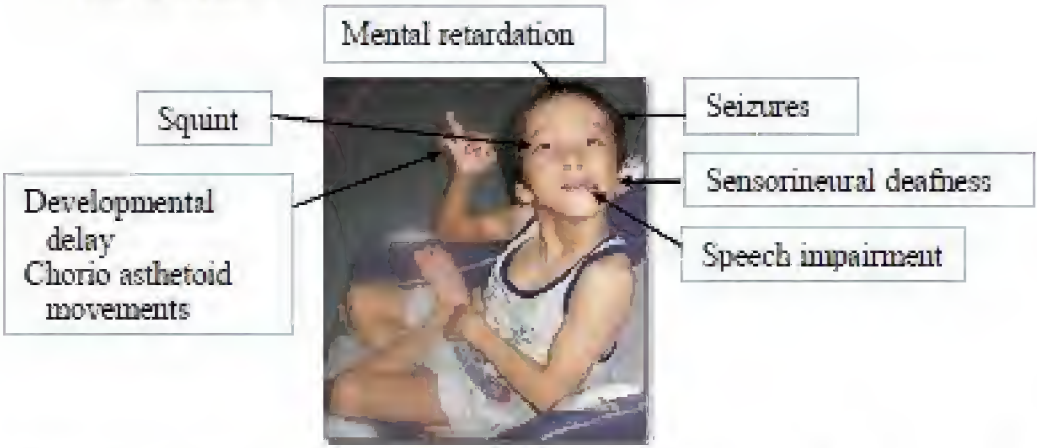


Many infants usually die during these phase

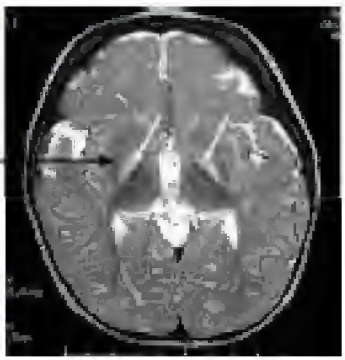
Survivors from previous phase go onto lucid interval for few months → there's apparent recovery or few symptoms.

B. Chronic bilirubin encephalopathy

- Picture of Cerebral Palsy become apparent by the 1st -3rd year of life
- Type : chorio asthetoid or spastic cerebral palsy
- Clinical features:



- MRI of a patient with chronic bilirubin encephalopathy (kernicterus) is shown, revealing the classic symmetric high-intensity signal in the globus pallidus (arrows).



Management

a- Prevention

* Adequate treatment of indirect hyperbilirubinemia (see before)
* Prevention and treatment of risk factors: e.g. sepsis, acidosis, asphyxia, …

b- Treatment

Acute

- Immediate Exchange Transfusion is mandatory once kernicterus is suspected
- Extensive phototherapy while waiting for exchange and after exchange
- Close monitoring of TSB and serum albumin to tailor further management plan
- Investigate for and treat risk factors e.g. sepsis ,anemia, cephalhematoma

Chronic

Not curable, need only supportive treatment for cerebral palsy.

Conjugated Hyperbilirubinemia

Definition: Rise of total serum bilirubin with the conjugated fraction > 15% of total Or > 2 mg/dl

Cholestasis: Means retention of conjugated bilirubin as well as other constituents of bile (e.g. bile salts)

Causes

1.Defective secretion of conjugated bilirubin by hepatocytes

a .Genetic - Rotor and Dubin Johnson syndrome

b. Acquired: (Neonatal hepatitis) due to:

* Infections : - Congenital infections e.g. TORCH
  - Neonatal sepsis.
  - Viral hepatitis : Echo, Herpes, EBV, Rarely HBV, HCV.
  - Idiopathic neonatal hepatitis
* Metabolic : - α_1 antitrypsin deficiency (13 %)
  - Galactosemia
  - Tyrosinemia

2. Defective excretion due to bile flow obstruction

∓ Intrahepatic:
- Congenital intrahepatic biliary atresia.
- Intrahepatic biliary paucity (hypoplasia) e.g. Allagile syndrome

∓ Extrahepatic:
- Congenital extrahepatic biliary atresia.
- Inspissated bile syndrome (Bile plug)

Clinical features

1. Color of sclera → Greenish or muddy yellow
2. Color of urine → Dark (bilirubinuria).
3. Color of stool → Pale (or clay).
4. Possible concurrent associations:
   - Hepatosplenomegaly.
   - Liver cells dysfunction.
   - Malabsorption and failure to thrive
   - Underlying systemic disease e.g. inborn error of metabolism, sepsis, TORCH.
   - No risk of kernicterus.

5. Timing

* In 1st day of life	- TORCH infection
* In the rest of 1st week of life	- Neonatal sepsis - TORCH infection
* Persistent during 1st month	- Neonatal hepatitis (metabolic or infections) - Congenital biliary atresia. - Inspissated bile syndrome

Investigations

- Liver function tests.
- Liver scan (HIDA scan).
- Liver biopsy.
- Metabolic screen for inborn errors of metabolism.
- TORCH screen.
- Sepsis screen

Treatment

i. Curable causes

- Sepsis → antibiotics.
- Galactosaemia → lactose free milk.
- Extra hepatic biliary atresia → Kasai operation (hepato-porto- enterostomy)

ii. Supportive

- Formulas with medium chain triglycerides
- Fat soluble vitamins
- Water soluble vitamins
- Bile acid binders (Cholestyramine) oral →↓serum chlosterol & bile acids.
- Minerals (e.g. calcium, phosphate).
- Liver transplantation for end stage liver failure.

Inspissated Bile Syndrome

- Persistent jaundice in newborns with elevations of both direct and indirect bilirubin after a period of increased indirect bilirubin
- It may be associated with massive hemolysis (Rh incompatibility), or hemorrhage (intraabdominal, intracranial, or retroperitoneal)
- Steroids & phenobarbitone may be tried in treatment

Haemolytic Disease of the Newborn (HDN)
(Erythroblastosis Foetalis)

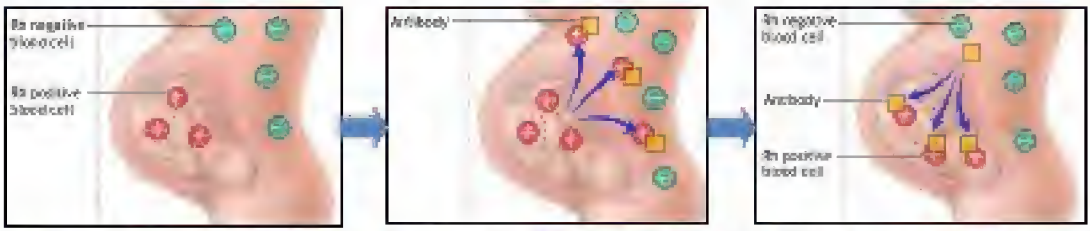
Etiology

Hemolysis of neonatal RBC's due to transplacental passage of maternal antibodies active against fetal RBCs. It includes:

1. Rh incompatibility; the mother is Rh negative and the baby is Rh positive
2. ABO incompatibility; the mother is usually group O and the fetus group A or B

Rh Incompatibility

Pathophysiology



- Escape of small amount of Rh +ve fetal blood (inherited from Rh +ve father) to the circulation of Rh –ve mother → maternal sensitization → formation of maternal anti-Rh antibodies (IgG) which crosses the placenta → Destruction of fetal RBCs
- The first baby usually escape hemolysis as sensitization usually occur near time of delivery, but the 1st baby may be affected if the mother was already sensitized e.g. with previous: - Amniocentesis
  - Blood transfusion
  - Chorionic villus sampling
  - Dead fetus (Miscarriage)
  - Ectopic pregnancy

Clinical features: According to severity; different presentations may occur:

1. **Severe hemolysis (Hydrops fetalis)**
   - Due to severe intrauterine hemolysis → severe anemia
   - Compensatory extramedullary hematopiosis→ huge hepatosplenomegaly.
   - Failure of compensation → anemic heart failure with:
     - Severe pallor.
     - Severe respiratory distress.
     - Massive generalized edema (skin, ascites , pleural effusion, pericardial effusion, polyhydramnios and placental edema)
     - Stillbirth or death short after birth

2. Moderate hemolytic; present by:-

- Anemia at birth worsening rapidly over the 1st day with hepatosplenomegaly
- Marked indirect hyperBilirubinaemia develops within few hours and progresses rapidly.
- Cases untreated usually die due to either kernicterus or anemic heart failure.

3. Mild hemolysis

- Mild hemolysis → mild anemia peaking at end of 3rd week.
- Unconjugated hyperbilinibinaemia at range of 16-20 mg/dl.
- May be splenomegaly.

Management

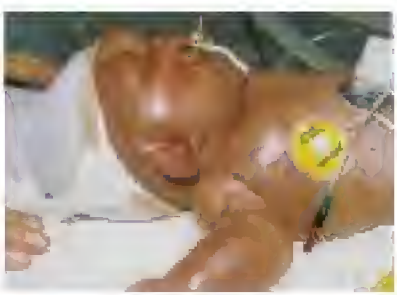
I. Postnatal management

Diagnosis : Immediately ,after the birth of any infant to an Rh-negative woman, Do:

- Blood group ABO and Rh
- Hemoglobin
- Baseline serum indirect bilirubin
- Direct Coombs test
- Monitor hemoglobin and indirect bilirubin every 6-8 hours

Management

1. For hydrops fetalis:



- Expert resuscitation
- Assisted /Mechanical ventilation
- Exchange transfusion with packed RBCs.
- Assist heart: Inotropes
- Correct hypoglycemia and hypocalcemia
- Correct acidosis

2. For indirect hyperbilirubinemia

A. Phototherapy in milder cases

B. Exchange transfusion

* Indications (see before)
* The blood used should be: Fresh and ABO-compatible with the mother and infant

3. Intravenous gamma globulin (inhibit hemolysis)

- Dose: 0.5gm/kg/dose; repeat in 12 hr
- Reduce the rate of hemolysis and the need for exchange transfusion in both ABO and Rh hemolytic disease

II. Antenatal management (Prevention)

A. First pregnancy

* IM Anti-D (RhoGam) is given provided:
  - The mother is Rh D negative
  - The fetus is Rh D positive
  - There is no maternal anti-D detectable in the mother's serum
* Regime:
  - One dose at 28 - 32 weeks' gestation
  - Another dose is given within 72 hours of delivery.
* Other situations e.g. ectopic pregnancy, threatened miscarriage
  - One or more Anti-D doses

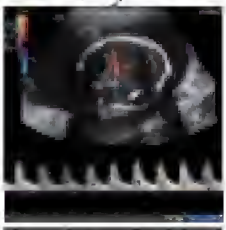
B. Subsequent pregnancies OR previous sensitization suspected

- Check anti-Rh.(anti D) titer in maternal blood by indirect Coomb's test Starting at 12-16 weeks gestation

↓

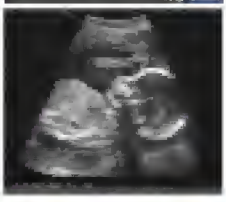
- If High OR rising titer → Check for fetal hemolytic disease by:

A. Doppler flow velocity of the fetal middle cerebral artery (in moderate to severe anemia it demonstrates an increase in the peak velocity of systolic blood flow)



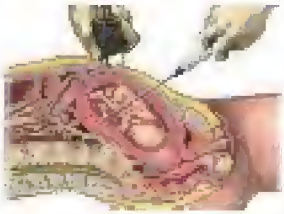
And

B. Ultrasonography for fetal well being and signs of hydrops



↓

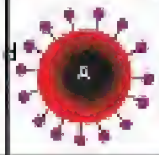
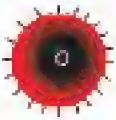
- If the infant appears to have severe anemia or Fetal hydrops before 35 weeks gestation



↓

Percutaneous Umbilical Blood Sampling (PUBS) is indicated to confirm hemolysis directly and if necessary, an intravascular fetal O negative Packed RBCs transfusion is given

ABO Incompatibility

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies present	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens present	 A antigen	 B antigen	 A and B antigens	None

Path physiology

- Occur when the mother blood group is O and the baby blood group is A or B.
- Maternal blood contain naturally present Anti-A and anti-B antibodies
- Maternal Anti-A and anti-B antibodies are usually of IgM type that is unable to cross the placental barrier, but in 10 % of cases these antibodies are of IgG type that can escape placental barier and affect the baby

Clinical criteria

- As antibodies are naturally present; the 1st baby may be affected
- Milder course
- Direct Coomb's test is weak positive
- Mild spherocytosis
- If ABO and Rh incompatibility coexist: Maternal preexisting anti-A or anti-B antibodies rapidly remove fetal Rh-positive cells from her circulation → mother is partially protected against sensitization

Treatment

- Phototherapy
- IVIG
- Exchange transfusions with type O blood of the same Rh type as the infant
- Some infants with ABO hemolytic disease may require transfusion of packed RBCs at several weeks of age because of slowly progressive anemia.

Self-assessment Quiz

Case 9

A 5-day-old, large-for-gestational-age, 4500-g boy has a bilirubin level of 15 mg/dL. There is no anemia or polycythemia. Examination apart from a moderate cephalohematoma is normal

a. **What is the diagnosis?**
b. **What is the required treatment?**

Case 10

Female newborn, second kid, aged 4 days, weight 3.900 kg, presented with neonatal jaundice noticed on the 3rd day of life. Examination reveal entirely normal adequately breast fed newborn, slight pallor, but no organomegaly

Investigations :

Indirect bilirubin level 19 mg/dl
Baby blood group A , Rh negative
Mother blood group O , Rh positive.
Baby hemoglobin 11 gm/dl

a. **Suggest a diagnosis**
b. **What are further investigations required?**

Case 11

A 6 days old, 36 week gestation male presents to his physician with worsening jaundice. He was discharged home on day 2 of life after successfully breastfeeding for a 24 hour period. At the time of discharge, his physical exam was unremarkable

Findings :

He is markedly jaundiced but otherwise normal
Fair urine output and yellow stools
Maternal and infant blood type is A +
The total bilirubin is 27 mg% with a direct fraction of 1 mg%
The hematocrit is 47% with a reticulocyte count of 1%

a. **What is the diagnosis?**
b. **Treatment?**

Case 12

This is a term female born by forceps assisted vaginal delivery to a primiparous woman , now she is 96 hours old ; she is not interested in feeding as before , sleepy all the time and has frequent eye staring and mouth twitches described as subtle seizures. Investigations

Indirect bilirubin level 26.5 mg/dl
Baby blood group A , Rh negative
Mother blood group O , Rh positive.
Baby hemoglobin 11 gm/dl
Reticulocyte count 5%

a. **What is the diagnosis?**
b. **What are the required investigations?**
c. **Management?**

Hemorrhagic disease of the newborn

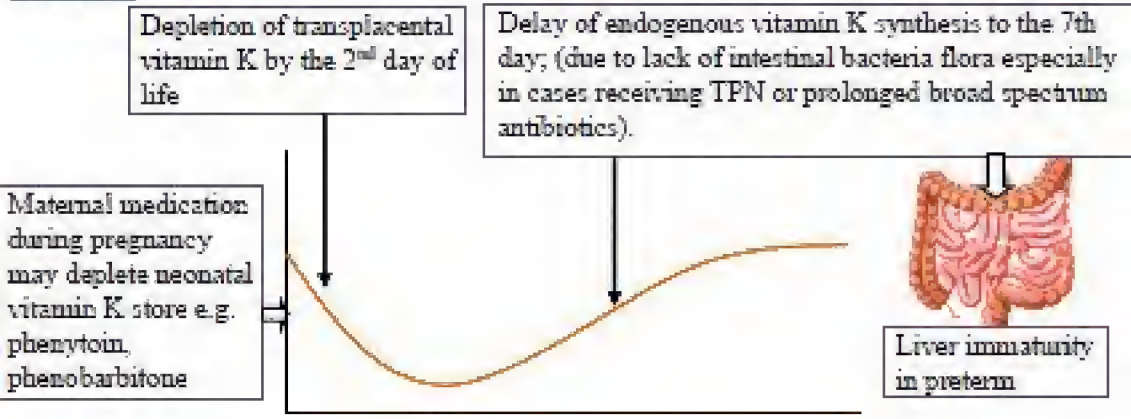
Definition

Hemorrhagic disorder in early neonatal period due to deficiency of vitamin K dependant clotting factors (II, VII, IX, X).

Incidence

- Affect about 2% of neonates not given vitamin K at birth
- Preterm and Breast milk feeders are more at risk than formula feeder full term.

Etiology



Clinical picture

1. Bleeding tendency:

* Timing?	– Usually between the 2nd - 7th day of life (may be early or late).
* Sites ?	– Commonly gastrointestinal, umbilical, or circumcision site – Rarely internal hemorrhage
* Look ?	– The baby looks well except if there is severe hemorrhage or intra cranial hemorrhage.

2. May be hemorrhagic anemia (pallor, tachycardia up to shock).

Investigations

- Prolonged prothrombin time (P.T.) and partial thromboplastin time (P.T.T)
- Deficiency of vitamin K dependant factors
- Normal bleeding time and platelet count

Prevention

- Vitamin K_1 1 mg , intra muscular at birth
- Oral vitamin K is less effective

Treatment

- Vitamin K_1 1-5 mg intravenous daily for 3 days
- Fresh plasma transfusion for preterm , liver diseases and active bleeding
- Fresh blood transfusion in severe bleeding.

Neonatal Anemia

Definition

A hemoglobin value less than the normal range of hemoglobin for birthweight and postnatal age

A. Physiologic anemia of infancy

At term

- Hemoglobin is 14-20 gm/dl (1-2 gm/dl lower in VLBW) and Htc. value 55% Due to relative intrauterine hypoxia→ ↑ erythropoietin →++ Bone marrow →higher hemoglobin at term
- As oxygen saturation improves after birth → ↓erythropiotine production→ Hemoglobin continue to decline to reach a nadir of 11 gm/dl at about 8-12 weeks of age (7-10 gm/dl in preterm)→ re stimulation of erythropiotine release .

Clinically

* Usually there is no clinically detectable pallor
* Anemia is self resolving, so usually requires no treatment

Prevention

Delayed clamping of the umbilical cord (≈1-2 min) with the infant held below the level of the placenta may enhance placental-infant transfusion and reduce postnatal transfusion needs; it provide extra 20-40 mL of blood and 30-35 mg of iron

B- Pathologic anemia

Blood loss	Hemolysis	↓ RBCs production
With normal reticulocyte count	With reticulocytosis	With reticulocytopenia
- Twin to twin transfusion	1. Immune hemolysis	- Congenital infections
- Feto-maternal transfusion	- Rh incompatibility	- Congenital leukemia
- Placental malformations	- ABO incompatibility	- Pure red cell anemia
After delivery	2. Hereditary hemolysis	
- Frequent sampling.	- Spherocytosis.	
- Neonatal hemorrhage whether internal or external	- G6PD deficiency - α-thalassemia	

Treatment

- Packed RBC's transfusion (15-20 ml/kg over 2- 4 hours)

Blood transfusion threshold depends on the severity of symptoms, hemoglobin level, and presence of co-morbid diseases (e.g. cyanotic congenital heart disease, respiratory distress syndrome) that interfere with oxygen delivery;

- At Hb% ≤ 11 for neonate on mechanical ventilation
- At Hb% ≤ 10 for neonate on minimal respiratory support

- At Hb% ≤ 8 for neonate on supplemental O_2 with poor weight gain or apnea
- At Hb% ≤ 7 for Asymptomatic neonate

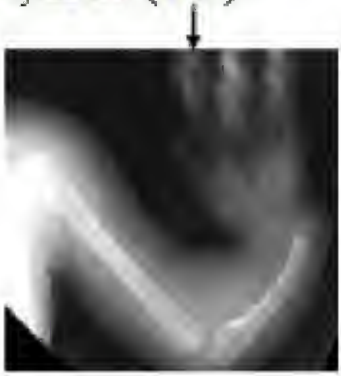
- Treatment of the cause e.g. Vitamin K for hemorrhagic disease of newborn

Neonatal bleeding

Causes

a. Bleeding in Otherwise Well Newborns

- Pseudohemorrhage in the Newborn
  - Fresh blood coming from the stomach of a newborn may be of fetal or maternal origin(swallowed maternal blood)
  - Apt test of the blood, based on maintenance of pink color of fetal but not adult hemoglobin diluted in1% sodium hydroxide, can help determine the origin of blood cells
- Platelet Disorders
  - Neonatal Alloimmune Thrombocytopenia (Maternal antibodies directed against fetal antigens)
  - Maternal Immune Thrombocytopenia Purpura
  - Congenital thrombocytopathy
  - Congenital Thrombocytopenia e.g.
    - Thrombocytopenia with absent radius syndrome (TAR)
    - Fanconi anemia (FA)
    - Wiskott Aldrich syndrome
- Hemophelias
- Vitamin K deficiency
- Local bleeding e.g. with NGT, thermometer



b. Bleeding in sick neonate

- Disseminated intravascular coagulation
- Liver disease
- Necrotizing enterocolitis
- Serious bleeding due to any cause

Workup

- Diagnosis and choice of an investigation depends on the newborn general condition , clinical pattern of bleeding , maternal and family history
- Basic workup includes:
  - Coagulation profile (PT ,PTT, D-Dimer)
  - CBC with blood film for platelet count and morphology
  - Specific e.g. specific clotting factor assay

Perinatal asphyxia

Definition

Acute or chronic impairment of gas exchange with hypoxia, hypercapnia and acidosis with consequent organ damage. The term Hypoxic Ischemic Injury (HII) has replaced the term of perinatal asphyxia

Causes

Impairment in oxygenation and perfusion due to

- Impaired placental supply due to placental insufficiency, placental abruption and uterine contractions
- Impaired umbilical supply due to cord compression/prolapsed or knots
- Impaired materno-placental supply due to maternal hypoxia or hypotension
- Impaired neonatal supply due to difficult delivery or inadequate resuscitation
- Post-natal causes (uncommon):
  - Severe congenital cyanotic heart diseases.
  - Severe anemia due to severe hemorrhage or severe hemolysis

Clinical picture

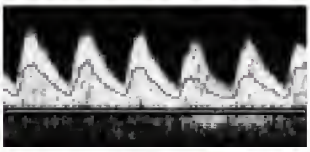
Depends on duration & severity of asphyxia

I. In the fetus

Indicators of fetal hypoxia and distress include:

1- Intrauterine growth restriction may indicate chronic hypoxia

2- Umbilical artery Doppler shows absent or even reversed end-diastolic flow suggesting severe fetal circulatory compromise

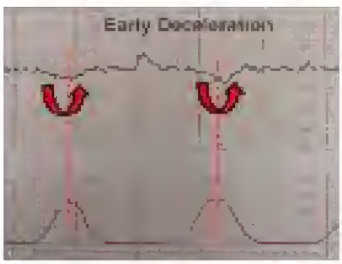


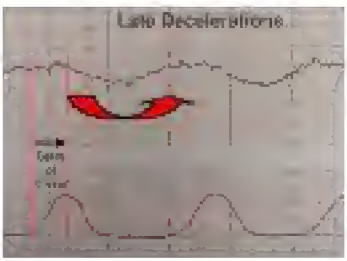
Normal end diastolic flow

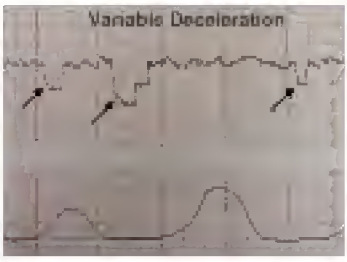
Absent end diastolic flow

Reversed end diastolic flow

3- Continuous heart rate recording may reveal a variable or late deceleration pattern (decrease in fetal heart rate beginning at or after the peak of the contraction and returning to baseline only after the contraction has ended)



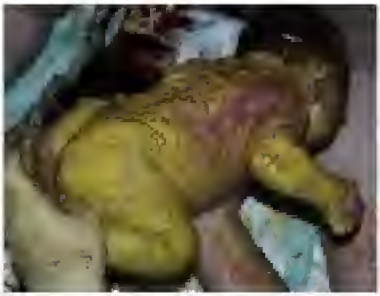




4- Acidotic scalp or cord pH

II. After delivery

1- Meconium staining of the newborn, amniotic fluid and vernix caseosa
2- Decreased consciousness and failure of spontaneous breathing.
3- Low Apgar score with cyanosis and flaccidity

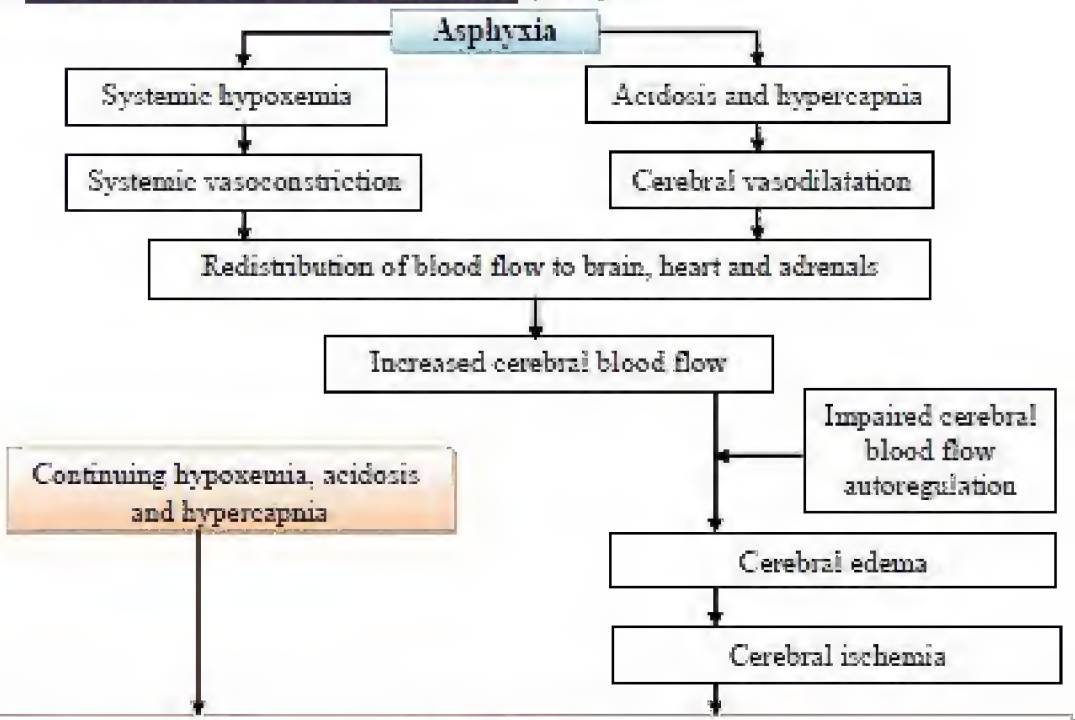


III. Later Neurologic and Multi Organ Dysfunction

American academy of pediatrics define severe asphyxia as combination of

- Low Apgar score < 4 for at least 5 minutes
- Umbilical artery pH < 7.00 (if obtained)
- Neurological insults e.g. seizures
- Multiorgan insults : Cardiac ,pulmonary ,renal or intestinal

1. Hypoxic-ischemic encephalopathy (HIE)



Brain cell injury

- Early phase (minutes – 6 hours)
  - Anaerobic glycolysis → intracellular energy failure→ necrotic cell death
  - Increased GABA
  - Release of excitatory amino acids particularly glutamate
- Late phase (6-72 hours)
  - Release of neurotoxic mediators e.g. free radicals and nitric oxide→apoptotic cell death

Sarnat and Sarnat clinical grading of HIE

Sign	Mild (I)	Moderate (II)	Severe(III)
○ Autonomic	Sympathetic	Parasympathetic	Depressed
○ Consciousness	- Hyper alert	- Lethargy	- Comatose
○ Muscle tone	- Normal	- Hypotonic	- Flaccid
○ Suckling reflex	- Weak	- Weak	- Absent
○ Moro reflex	- Exaggerated	- Weak	- Absent
○ Pupils	- Dilated	- Miotic	- Often unequal
○ HR	- Tachycardia	- Bradycardia	- Variable
○ Seizures	- None	- Common	- Decerbrate
○ EEG	- Normal	- Abnormal	- Abnormal (isopotential)
○ Duration	1-3 days	2-14 days	- Hours to weeks
○ Out come	Good	Variable	- Death or severe deficits

2. Cardiac → Heart failure, cardiogenic shock

3. Respiratory → Meconium aspiration ,apnea, pulmonary hypertension

4. Renal → Oliguria, hematuria, Acute tubular necrosis

5. GIT →Necrotizing enterocolitis

6. Hematologic → DIC

6. Metabolic →Hypoglycemia , hypocalcemia ,hypomagnesemia, hyponatremia and syndrome of inappropriate secretion of ADH

Diagnosis :

There are no specific tests to neither confirm nor exclude a diagnosis of HII
Diagnosis is made based on the history, physical and neurological examinations

1. Neuro imaging

- Brain MRI
  - Modality of choice for the diagnosis and follow-up of HIE
  - Early detection of brain edema and brain injury (basal ganglia)
  - Conventional MRI show changes by the 3rd day
  - Diffusion Weighted MRI shows changes in the 1st 24 hours (*preferred*)
- Cranial ultrasonography
  - Less sensitive than MRI (initial scan is negative in up to 50% of cases)
  - Perform on day 1 then as guided by clinical condition

2. EEG

- Both standard EEG and amplitude integrated (aEEG) are used
- Detects seizures and evaluate the degree of encephalopathy

Management

A. In delivery room

1- Avoid and treat risk factors
2- If fetal distress: provide high flow oxygen & prepare for immediate delivery
3- Neonatal resuscitation according to neonatal life support guidelines
4- Assess severity of encephalopathy

B. In NICU

1. Therapeutic Hypothermia

Idea: Moderate hypothermia in perinatal asphyxia is neuroprotective

Neuroprotection via:

- Reduced metabolic rate and energy depletion
- Decreased excitatory transmitter release
- Reduced apoptosis
- Reduced vascular permeability, and edema.

Eligibility

- ≥ 36 weeks gestation
- < 6 hours old
- Evidence of moderate to severe encephalopathy (Sarnat)
- Evidence of perinatal asphyxia; one of the following
  - Apgar ≤ 5 at 10 minutes
  - Continuing resuscitation at 10 minutes
  - pH < 7.00 in the first hour
  - Base Excess ≤ - 16 in the first hour

Method

- Resuscitation as usual
- Start selective head cooling (using CoolCap) or total body cooling (systemic).
- Rectal temperature is then maintained at 34-35°C for 72 hours.
- Rewarming is carried out gradually, over 6-8 hours.

2. Supportive care

Ventilation

- Consider ventilatory support early
- Ensure adequate oxygenation; avoid hyperoxia
- $PaCO_2$ between 35 - 45 mmHg is neuroprotective
- Treat pulmonary hypertension if exist

Cardiovascular

- Consider invasive blood pressure monitoring
- Maintain mean arterial blood pressure above 35-40 mm Hg in term to ensure adequate cerebral perfusion
- Consider inotropic support early ; start with dobutamine infusion and add dopamine if required
- Fluid boluses if hypovolemic
- Monitor Hb% ; acute fall may indicate new intracranial hemorrhage
- ECG and Echo if there is concern over poor cardiac function

Fluids

- Fluid balance based on weight, urine output, serum sodium & renal function
- Initially fluid restrict to 60-80 % maintenance and liberalize as urine output improve

Neurology

- Treat seizures even asymptomatic (i.e., seen only on EEG)
- Phenobarbitone is the drug of choice

Metabolic

- Maintain normoglycemia
- Treat hypocalcemia

Coagulation

- Send coagulation screen; PT, PTT, D-dimer and platelets
- Correct any coagulopathy with Vit K ,FFP, cryopreciptate or platelets

Feeding

- Withhold enteral feeds for the first 3 days
- Introduce feeds cautiously when clinical condition has improved
- Increase feed volumes slowly
- Monitor for necrotizing enterocolitis

Withdrawal of care

- May be appropriate for severe HIE who have iso electric/burst suppression in EEG and abnormal cerebral blood flow on Doppler
- Active treatment should be continued at least for the first 24 hours

Prognosis

About 20-30% of infants with HIE die in the neonatal period
≈ 33-50% of survivors are left with permanent neurodevelopmental abnormalities (cerebral palsy, mental retardation).

Neonatal Seizures

Definition

Paroxysmal alterations of neurologic functions including motor, behavioral and / or autonomic changes

Causes

A. Central nervous system

- Incidence: the commonest causes, includes:
  - Hypoxic-ischemic encephalopathy (the commonest cause in term babies).
  - Intra cranial hemorrhage (intraventricular, parenchymal, subarachnoid or subdural)
  - Sepsis (meningitis, encephalitis, tetanus, TORCH)
  - Congenital brain malformations e.g. cerebral dysgenesis (5%).
  - Bilirubin encephalopathy (Kernicterus)
  - Neuro-cutaneous syndromes e.g. tuberous sclerosis, incontinentia pigmenti

B. Metabolic

1. Hypoglycemia
   - Blood glucose less than 2.6 mmol/l (≈ 45 mg/dl)
   - Causes: infant of diabetic mother (IDM), preterm, asphyxia , hypopituitarism, Erythroblastosis fetalis, galactosemia
2. Hypocalcaemia
   - Serum calcium less than 7mg/dl which either:
     - Early onset (in 1st 3 days) → due to IDM, preterm, & asphyxia.
     - Late onset (after end of 1st week) → due to decrease calcium intake, hyper phosphatemia, and hypoparathyroidism.
3. Hypomagnesemia (< 1.5 mg/dl) → often associated with hypocalcaemia
4. Hyponatraemia (< 135 meq/L) or hypernatraemia (> 150 meq/L)
5. Inborn errors of metabolism: e.g.
   - Galactosemia
   - Hyperammonemia
   - Organic acidemia

C. Other causes

- Pyridoxine or pyridoxal (vitamin B6) dependency (essential for GABA)
- Drug withdrawal e.g. maternal narcotics or addiction
- Theophylline toxicity
- Benign neonatal seizures (normal neonate ;diagnosed by exclusion)

Clinical picture

Subtle seizures

The commonest type (50 %) occurs more commonly in premature than full term:

- Eye movements: eye rolling, eye deviation, staring, blinking or nystagmus
- Repetitive oral movements: suckling, chewing or lip smacking.
- Limb movements: pedaling, bicycling or boxing
- Autonomic: apnea, fluctuations in heart rate, hypertension episodes & desaturations

Clonic seizures

- Limb jerking
- Multifocal (rarely generalized due to decreased connectivity associated with incomplete myelination in neonates)

Myoclonic seizures

- Brief sudden, shock like jerking movements of limbs

Tonic seizures

- Focal: persistent posturing of a limb or trunk or neck often with persistent horizontal eye deviation.
- Generalized: bilateral tonic limb extension or tonic flexion of upper extremities often associated with tonic extension of lower extremities

Spasms

- Very brief sudden generalized jerks lasting 1-2 sec
- Distinguished from generalized tonic spells by their shorter duration

Approach to diagnosis

a. History

- Onset of convulsions
  - * In the 1st 4 days of life: e.g. HIE, drug withdrawal, or metabolic causes.
  - * After the 4th day: e.g. intra cranial hemorrhage and metabolic causes.
  - * After the 1st week:: e.g. sepsis (meningitis).
- Course and duration of convulsions
- Perinatal insults:
  - Maternal diseases, medications or addiction
  - Birth trauma
  - Evidence of asphyxia
- Family history for benign neonatal seizures or inborn errors of metabolism

b. General examination

- Search for cranial birth trauma or congenital head anomalies
- Signs suggestive of sepsis or congenital infections

- Severe hyperbilirubinemia plus risk factors→ kernicterus
- Abnormal Smell → metabolic causes
- Skin examination e.g. for hypomelanotic patches of tuberous sclerosis
- Retinal examination for chorioretinitis in TORCH

c. Neurologic examination

- Pattern of convulsions
- Signs of raised intra cranial tension e.g. tense fontanel

Investigations

- Check initially for blood glucose, calcium, magnesium, sodium, blood gases
- Sepsis Screen: complete blood picture, CRP, blood culture.
- CSF analysis: - For glucose, protein, Gram stain, culture and viral PCR
  - Delay lumbar puncture if the baby is unstable
- TORCH Screen for suspected cases
- Neuro imaging : - Cranial ultrasound excludes intra cranial hemorrhage
  - CT/MRI for brain malformations, and infarcts
- Electroencephalogram (EEG)
- Metabolic Screen if acidotic or family history: e.g. ammonia, amino acids, lactate, urine amino acids and organic acids
- Karyotyping for dysmorphic babies

Differential diagnosis

Seizures should be differentiated from **Jitteriness** which is characterized by:

- Tremor like movements of limbs
- Precipitated by sensory stimuli.
- Stopped by holding the limb.
- No associated autonomic changes, ocular phenomena or EEG changes
- Seen in normal infant, drug withdrawal, hypocalcemia & hypoglycemia

Treatment

- Maintain ventilation which may be compromised during seizures and following anti convulsants
- Rapidly identify and treat reversible causes of seizures

- Hypoglycemia	→ Glucose 10% I.V 2- 4 ml/kg
	→ May require continuous glucose infusion
- Hypocalcemia	→ Calcium gluconate 10% slow I.V 2 ml/kg
- Hypomagnesemia	→ Magnesium sulphate 50% I.M 0.2 ml/kg

- Start parenteral antibiotics (± acyclovir) if there is any concern of sepsis

- **Anti convulsants**

Start an anticonvulsant if → Seizure lasting > 5minutes
→ Brief but frequent seizures > 3 /hour
→ Prolonged desaturations
→ Hemodynamic instability

First line: Phenobarbitone

- Loading dose 20 mg/kg IV
- If seizures continue at 30 minutes→ give another 10 mg/kg IV and take blood for phenobarbitone level (Therapeutic phenobarbital levels are 20-40 µg/mL)
- If seizures remain uncontrolled → give further 10mg/kg IV (total 40 mg/kg)

If total loading dose of 40 mg/kg of phenobarbitone was ineffective

Second line : Phenytoin

- Loading dose 20 mg/kg slow IV over 30 minutes
- Monitor heart rate and blood pressure closely
- Better avoided in babies with poor cardiac function

Third lines

Lorazepam

- 0.05 mg /kg IV repeated every 6-8 hours
- Usually, it does not cause hypotension or respiratory depression

Midazolam

- 0.05-0.1 mg/kg IV, with a continuous infusion of 0.5-1 micg/kg/min IV
- Carry risk of hypotension and respiratory depression

If poor response to previous treatment

Therapeutic trials

- Pyridoxine or pyridoxal phosphate 100-200 mg IV with real time EEG
- The seizures abruptly cease, and the EEG normalizes in the next few hours
- If there is negative response to IV pyridoxine ,try:
  - 1 week trial of pyridoxine 100 mg oral daily
  - 6 weeks of pyridoxal phosphate 30 mg/kg oral daily
  - Creatine 300 mg/kg daily + Folinic acid 2.5 mg bid + Biotin (10 mg od)

Maintenance treatment

- If seizures persist, use phenbarbitone 3-6 mg /kg in 2 divided doses started 24 hours after the loading dose
- Most will have stopped anticonvulsants except those with abnormal neurology

Self Assessment Quiz

Case 13

A 4 days male infant presented in the outpatient department with bleeding from circumcision site. The child was the product of a full-term, normal pregnancy in a 25 year old mother with an uncomplicated antenatal period. Family history was negative for any form of hereditary or acquired bleeding disorder. He was delivered by spontaneous vaginal delivery at home without any intervention and was on exclusive breast feeds. Prothrombin time (PT) and partial thromboplastin time (PTT) done at that time were markedly elevated with hemoglobin 11.5 gm/dl

a. **What is the most likely diagnosis?**
b. **What are the 3 most important lines of treatment?**

Case 14

A full-term infant is born after a normal pregnancy; delivery, however, is complicated by marginal placental separation. At 12 h of age, the child, although appearing to be in good health, passes a bloody meconium stool.Intramuscular vitamin K was administered in the delivery room. Clinically the baby was well and all clotting indices and hemoglobin were normal

a. **What is the expected diagnosis?**
b. **How to confirm?**

Case 15

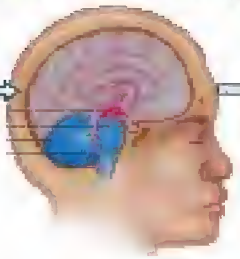
A female baby was born at 38 weeks of gestation by spontaneous delivery. Birth weight was 3470 g and Apgar score 1/3/3 (at 1 minute,5 minutes and 10 minutes). After delivery, the baby needed immediate cardiopulmonary resuscitation with intubation, external cardiac massage, ventilatory assistance and an immediate blood transfusion for severe anemia (Hb 2.5 g/dL). Severe metabolic acidosis was present (pH 6.81), with arterial hypotension (41/19 mmHg)

a. **What is the clinical scenario?**
b. **How can you predict neurologic outcome?**

Causes of Neonatal Respiratory Distress

I. Central

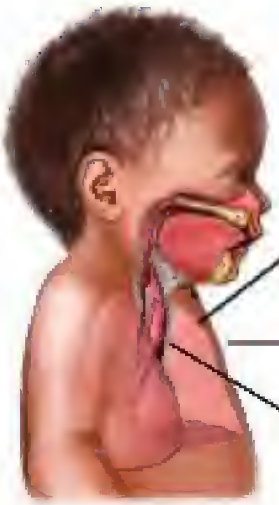
CNS failure: Due to
- Over sedation
- Perinatal asphyxia
- Intra cranial hemorrhage



Manifested by:
- Slow, irregular, gasping respiration.
- Apneic attacks.
- Disturbed consciousness.
- Poor reflexes

II. Peripheral

A. Pulmonary



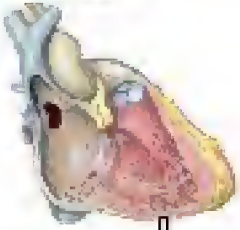
Lungs
- Transient tachypnea of newborn (TTN)
- Respiratory distress syndrome (RDS)
- Meconium aspiration syndrome (MAS)
- Congenital pneumonia
- Congenital lobar emphysema
- Lung collapse, Cysts, Hypoplasia

Pleura
- Air leak e.g. Pneumothorax
- Congenital diaphragmatic hernia (CDH)
- Pleural effusion.

Airways
- Vascular ring
- Bilateral choanal atresia

B. Extra Pulmonary

1. Cardiac

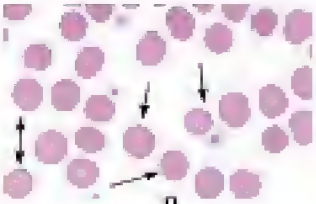


- Heart failure
- Duct dependent Congenital heart diseases
- Critical obstructive lesions

2. Metabolic

- Metabolic acidosis
- Hypoglycemia
- Hypothermia

3. Hematologic



- Anemia
- Polycythemia

Clinical signs of peripheral respiratory distress

Grade I	(Mild)	→	Tachypnea (> 60 / min) & working alae nasi
Grade II	(Moderate)	→	As mild plus intercostal & subcostal retractions
Grade III	(Severe)	→	As moderate plus grunting
Grade IV	(Advanced)	→	As severe plus central cyanosis, disturbed consciousness

Initial management of babies presenting with respiratory distress

1. Resuscitation and ensure temperature stability
2. Pulse oximetry and supplemental oxygen
3. Chest radiograph : immediate if significant respiratory distress or delayed until 4 hours if mild respiratory distress
4. Review history : gestation, rupture of membranes, type of delivery, meconium stained amniotic fluid, maternal diabetes
5. If RDS suggested consider intubation and early surfactant and/ or CPAP
6. Assess for clinical improvement regarding:
    - Well/ unwell, pink/pale/blue
    - Perfusion
    - Signs of respiratory distress
    - Oxygen saturation

- Clinical improvement →observe over 10 - 20 minutes → if quiet tachypnea → consider TTN → routine neonatal care
- Consider echocardiography if lung fields in chest radiograph is clear
- Proceed to further support if any of the following exists:
    1. No clinical improvement
    2. Condition deteriorates
    3. Abnormal chest radiograph
    4. Infant requires > 40% oxygen to maintain saturation

- Establish IV access
  - Umbilical venous catheter and start IVF 60 ml /kg/day initially 10% dextrose
  - Consider umbilical arterial catheter for blood pressure monitoring and ABG analysis if the infant's inspired fraction of oxygen exceeds 40%
- Blood tests
    - Blood glucose
    - CBC with differential
    - CRP
    - Blood culture; Not helpful initially as results may take 48 hours
    - Blood gases
- Start IV antibiotic : Benzylpenicillin (or Amoxicillin) and Gentamicin

Respiratory support (see RDS)

Respiratory Distress Syndrome (RDS)

(Hyaline membrane disease)

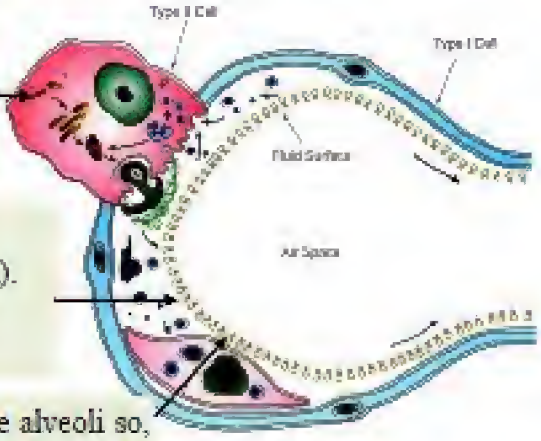
Definition

A syndrome of respiratory distress occurs almost exclusively in premature due to surfactant deficiency

RDS is the commonest cause of neonatal death.

Surfactant

A lipoprotein produced by alveolar cells type II starting after 20th week of gestation and mature after 35th weeks (near term).



Composed mainly of:
- Dipalmitoyl phosphatidylcholine (Lecithin).
- Phosphatidyl glycerol.
- Surfactant proteins A, B ,C& D

Functions: reduce surface tension within the alveoli so, prevent their collapse at the end of expiration and reduce the lung stiffness and work of breathing

Causes of RDS

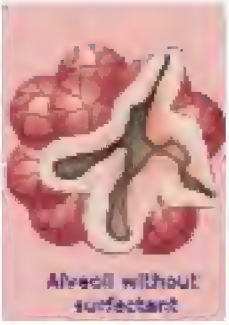
1. Prematurity
   - The leading cause of RDS
   - Incidence & severity of RDS are related inversely to the gestational age of the newborn infant e.g. about 60% of prematures < 28 weeks develop RDS
2. Infant of diabetic mother
   - Fetal cortisone is essential for surfactant production
   - Maternal hyperglycemia → fetal hyperinsulinemia→ ↓↓ fetal cortisone
3. Cesarean section(CS) and precipitate labor:
   - Due to lack of stressful delivery → reduced fetal cortisone.
4. Intrapartum asphyxia
   - Due to hypoxemia of alveolar cells type II.
5. Others : Second twin, male Sex, RDS in Siblings

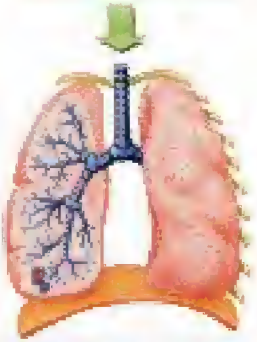
In contrast, the incidence of respiratory distress syndrome decreases with the following:

- Use of antenatal steroids
- Pregnancy-induced or chronic maternal hypertension
- Prolonged rupture of membranes
- Maternal narcotic addiction

Pathophysiology

1. ↓ Surfactant →↑ alveolar surface tension → diffuse alveolar collapse during expiration





2. Low lung compliance (higher pressure is required to initiate lung inflation)→increased work of breathing → respiratory distress

3. Impaired gas exchange with
   ⇩
   Hypoxemia
   Hypercapnia
   Respiratory acidosis

4. Hypoxemia→ alveolar cells type II dysfunction→ more surfactant deficiency → Progressive atelectasis

Clinical picture

- Progressive signs of respiratory distress are noted soon after birth and include the following:
  - Tachypnea
  - Nasal flaring
  - Expiratory grunting (from partial closure of glottis)
  - Subcostal and intercostal retractions
  - Cyanosis
  - Extremely immature in neonates may develop apnea and/or irregular respirations
  - Patients may also have edema, ileus, and oliguria

- **Course**
  - Endogenous surfactant production usually become sufficient by 48-72 hours→ Clinical improvement is often heralded by spontaneous diuresis and improved blood gas values at lower inspired oxygen levels and/or lower ventilator support
  - Severe cases may end in death or complications

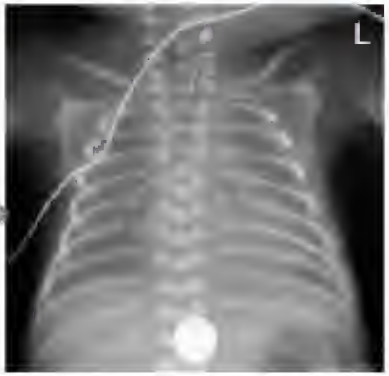
Diagnosis

1. Clinical

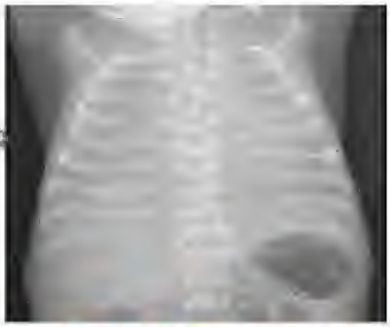
RDS is suspected clinically in cases with early respiratory distress in presence of risk factors particularly prematurity

2. Chest radiographs

A. Mild to moderate RDS
- Bilateral, diffuse, reticulo- granular infiltrates (ground-glass appearances)
- Air bronchograms represent aerated airways superimposed on a background of collapsed alveoli
- Poor lung expansion (small lungs volumes)

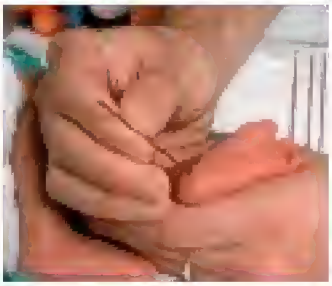


B. Severe RDS
Opacification of both lungs (White airless lungs)



3. Blood gases analysis

- In Milder RDS: Hypoxemia
- In Severe RDS: Hypoxemia + Hypercapnia + Respiratory acidosis



4. **Sepsis workup**: blood cultures, a complete blood count with differential, and C-reactive protein

Fetal lung maturity tests

Prediction of fetal lung maturity is derived by:

1. Estimating Lecithin/sphingomyelin ratio in the amniotic fluid :
   * If > 2 → Mature lung → No risk of RDS
   * If 1.5-2 → Transitional lung → Risk of RDS
   * If < 1.5 → Immature lung → Severe RDS
2. The presence of phosphatidylglycerol in the amniotic fluid→ No risk of RDS

Differential diagnosis

Other causes of early neonatal respiratory distress e.g.
Early-onset sepsis (GBS pneumonia)
Cyanotic heart disease

Prevention of RDS

- Antenatal steroids to enhance pulmonary maturity & surfactant production
  - Recommended for:
    - Threatened preterm labour between 24-34 weeks gestation
    - Preterm premature rupture of membranes
    - Any condition requiring elective preterm delivery
  - Use : Betamethasone or dexamethasone
  - Protocol: 2 doses are given 12hours apart
- Control Risk factors e.g. maternal diabetes
- Expert Resuscitation
- Early alveolar Recruitment by immediate use of *nasal CPAP*
- Early administration of surfactant

Treatment of RDS

A. Supportive measures

- Incubator care in NICU and Respiratory support (See Before)
- Temperature : goal core temperature = 36.5 – 37 C
- Nutrition :
  - Start with glucose 10 % and aminoacids (in exteremly prematures) at rate of 65-75 ml /kg; increase gradually over the first week to 150-180 ml/kg ; avoid overhydration that may open ductus arteriosus
  - Electrolytes added at 2-3rd day
  - Monitor electrolytes and urine output

Respiratory Support

Aim:

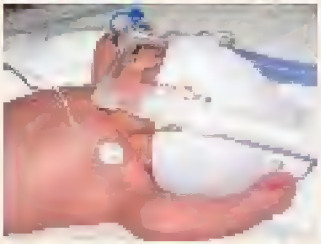
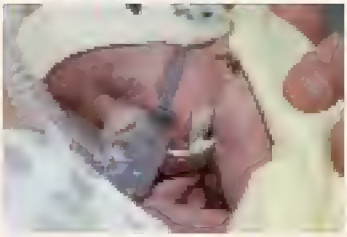
- Keep arterial oxygen pressure between 50 and 70 mm Hg
- The currently recommended range of oxygen saturation targets is 91-95%.

I. Ambient /head box /nasal cannula / Vapotherm

If baby looks comfortable with good saturation and good blood gases (pH >7.25 and PCO2 < 50 mmHg)

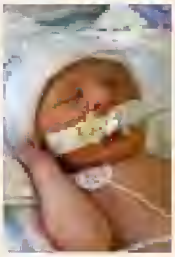
II. Nasal Continuous Positive Airway Pressure (nCPAP)

- Recruits and prevents collapse of surfactant-deficient alveoli
- Early use of CPAP for stabilization of at-risk preterm infants beginning as early as in the delivery room reduces ventilatory needs
- Considered if oxygen saturation cannot be kept > 90% at inspired oxygen concentrations of 40-70% or greater
- Another approach is to intubate the preterm infant, administer intratracheal surfactant and then extubate the infant and begin CPAP.
- If an infant with RDS undergoing CPAP cannot keep oxygen saturation >90% while breathing 40-70% oxygen, assisted ventilation and surfactant are indicated

III. Endotracheal intubation (and Surfactant) and Mechanical Ventilation

- Consider for any of the following
  - Baby unwell, marked recessions
  - No improvement on CPAP :CPAP of 5-10 cm H_2O cannot keep oxygen saturation > 90% while breathing 40-70% oxygen
  - Infants with respiratory failure
    - Arterial blood pH <7.20
    - Arterial blood $PaCO_2$ of ≥ 60 mmHg
    - Arterial blood PaO_2 of < 50 mmHg




IV. Surfactant

- Prophylactic treatment
  - Indicated for very low birth weight < 30 weeks
  - In the first few minutes of life before clinical or radiologic confirmation of RDS
- Rescue treatment
  - For babies ≥ 30 weeks
  - Surfactant administered to ventilated infants with clinical and or radiological signs of RDS

Types

- Natural

Suvanta (Bovine surfactant)	○ 4mL/kg (100mg/kg) ○ Repeated if necessary every 6h (up to 4 doses)
Curosurf (Porcine surfactant)	○ Initial dose 2.5mL/kg (200mg/kg) ○ Followed if necessary by 1.25mL (100mg)/kg after 12 hours and 24hours

- Synthetic: Surfaxin which mimic human surfactant

Protocol

- ○ Injected intra tracheal via endotracheal tube
- ○ Observe the baby and ventilator settings closely for 30 minutes after the dose
- ○ Repeat blood gases after 30 minutes
- ○ Avoid EET suction for 1-4 hours if possible
- ○ Consider subsequent doses if
  - Baby has high or increasing ventilator parameters after the 1st dose
  - FiO_2 > 30% despite adequate ventilator parameters

Side effects

- Bradycardia and desaturation
- Pulmonary hemorrhage
- Air leaks ; Pneumothorax

B. Antibiotics

- ○ Start antibiotics in all infants who present with respiratory distress at birth after the sepsis screen have been obtained.
- ○ Discontinue antibiotics after 2-5 days if blood cultures are negative and no maternal risk factors found

Complications of RDS

Disease related

- Patent ductus arteriosus (PDA) and heart failure
- Intraventricular hemorrhage (IVH)

Treatment related e.g.

- Bronchopulmonary dysplasia (BPD)
- Retinopathy of prematurity (ROP)

Prognosis: Inversely proportionate to gestational age.

Transient Tachypnea of Newborn

- Commonest self-limited respiratory distress in full term
- Due to delay in clearance of fetal lung liquid

Risk factors

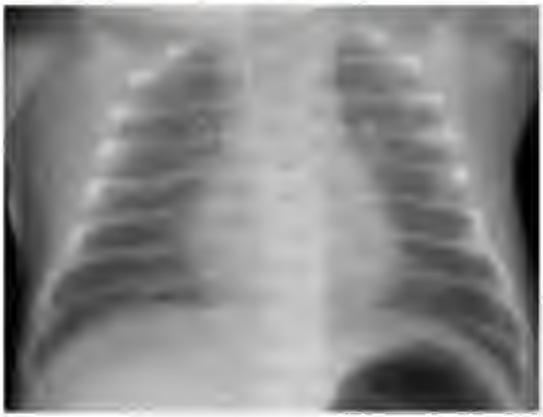
- Cesarean section
- Maternal asthma and smoking
- Maternal diabetes
- Maternal excess analgesia
- Perinatal asphyxia

Clinical picture

- Mild respiratory distress (tachypnea) within few hours after birth
- The chest generally sounds clear without rales or rhonchi ("quiet" tachypnea)
- Spontaneous resolution usually occur within 72 hours

Chest X-ray

- Prominent perihilar streaking, which correlates with the engorgement of the lymphatic system with retained lung fluid
- Fluid in the fissures
- Hyperinflated lung& mild cardiomegaly



Treatment

Supportive care as before

1- Provide oxygen as needed

2- Antibiotics

3- Infants with significant distress have poor bowel motility and require IV fluids

N.B Hyperactive airway and chest wheezing is common in later life

Meconium Aspiration Syndrome

- Meconium-stained amniotic fluid (MSAF) occurs in about 15 % of deliveries
- Not all neonates with MSAF develop meconium aspiration syndrome (MSA)
- MAS occurs only in 5 % of infants with MSAF

Pathophysiology

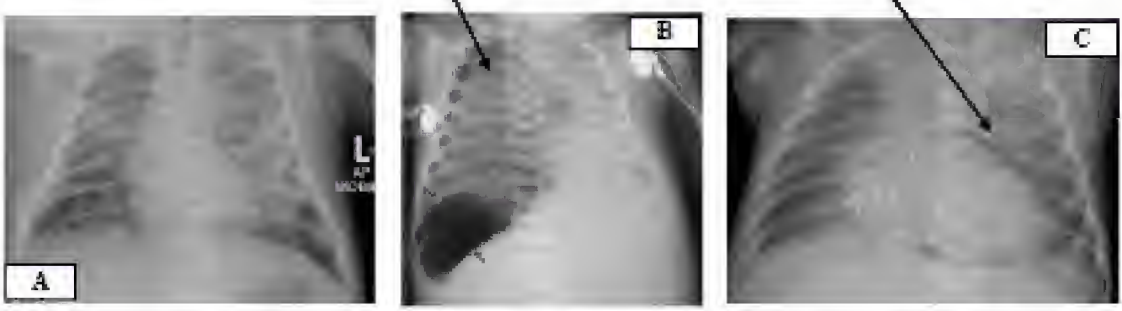
1. Factors that promote the passage of meconium in utero include the following:
    - Perinatal asphyxia
    - Oligohydramnios
    - Maternal infection/chorioamnionitis
2. Meconium may be aspirated before, during, or just after birth
3. Outcome of meconium aspiration:
    - Complete airways obstruction→ Patchy collapse
    - Incomplete airways obstruction → Air trapping.
    - Secondary infection & chemical pneumonitis→ Surfactant dysfunction
    - Pulmonary hypertension

Clinical picture

- MAS occur typically in term and post-term infants
- Skin, nails and umbilical cord may be meconium stained
- Signs of severe respiratory distress with grunting and cyanosis
- Barrel chest in the presence of air trapping
- Auscultated rales and rhonchi (in some cases)
- May have signs of neonatal encephalopathy

Chest radiograph

- Hyperinflated chest with patchy consolidations and collapse (A)
- May be air leak e.g. pneumothorax (B) , pneumopericardium (C)



Management

A. management of meconium stained baby in the delivery room

Vigorous active neonate
- Breathing /crying
- HR >100/minutes
- Good tone

No
- Baby is flaccid
- Apneic
- Bradycardic

- No initial respiratory stimulation
- No bag and mask ventilation
- Rapid and brief Oro/hypopharyngeal suction to improve visualization of vocal cord
- Immediate laryngeoscopy and tracheal suction through EET with ambient oxygen all through the procedure

Yes

- Thorough oropharyngeal suctioning with wide bore catheter
- Provide warmth
- Sniffing position
- Supplemental O_2 as needed
- Nasal and gastric suctioning of amniotic fluid

Routine resuscitation as needed

B. Treatment of MAS

- Respiratory support in NICU as before
- Consider early mechanical ventilation (high oxygen, high rate, long expiratory time ,low pressures, use sedation)
- Antibiotics
- Surfactant
- High frequency ventilation for severe MAS

Neonatal Cyanosis

Definition

- Bluish discoloration of skin and mucus membranes due to presence of more than 5 gm/dl reduced hemoglobin in capillary blood.

Causes

1. Peripheral: with e.g. shock, hypothermia and acrocyanosis
2. Central
   A. Pulmonary e.g.
      - Severe RDS
      - Severe MAS
      - Congenital diaphragmatic hernia

   B. Cardiac

   Congenital cyanotic heart diseases (CCHD) e.g.
      - Transposition of great arteries
      - Tricuspid atresia
      - Tetralogy of Fallot
      - Total anomalous pulmonary venous return

   C. Hematologic
      - Polycythaemia
      - Methemoglobinemia(congenital or acquired)

Differential diagnosis

1. Cardiac causes → Emergency echocardiography
2. Hyperoxia test

   Differentiate between pulmonary & cardiac causes of cyanosis if emergency Echo is not readily available
   - Perform arterial blood gases in room oxygen then give 100% O_2 and perform arterial blood gases again
   - If PaO_2 become > 150 mmHg after 100% O_2 → pulmonary cause of cyanosis.
   - If PaO_2 remain below 100 mmHg despite 100% O_2 → cardiac cause of cyanosis; These patients should receive PGE1 infusion to maintain ductus arteriousus patent.
3. Blood examination → for polycythemia & methemoglobinemia

Neonatal Apnea

Definition

- Pauses in breathing for > 15 seconds
- Apnea > 20 second is associated with bradycardia and desaturation

Etiology

1. Apnea of prematurity: causes

- Central (40%) : due to immaturity of respiratory centers
- Obstructive (10%) ; upper air way obstruction e.g. neck flexion
- Mixed (50%)

2. Systemic diseases

- Sepsis
- GORD
- Anemia /polycythemia
- Intra ventricular hemorrhage (IVH)
- Electrolyte disturbances /hypoglycemia
- Hypothermia
- Drugs e.g. sedation, prostaglandins
- Disorders e.g. RDS, PDA, NEC, Pierre – Robin sequence

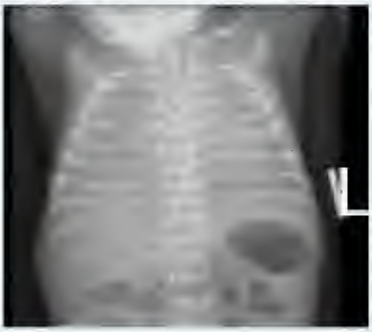
Treatment

- Investigate and treat any possible underlying cause e.g.
  - Full sepsis screen and start broad spectrum antibiotics
  - GORD: ensure correct NG tube position, positioning the baby with head up tilt, prone or lateral, reduce feed volume and increase frequency, feed thickener and anti GOR medications
- Cardio respiratory monitoring
- Apnea chart to document frequency and severity of apnea.
- Interventions for apnea with bradycardia and desaturations:
  - Tactile stimulation
  - Supplemental oxygen
  - Gentile oral suction
  - Positioning: to avoid extreme flexion or extension of the neck
  - Respiratory stimulants: started in the 1st few days of life for those <30 wks
    - Aminophylline
    - Caffeine citrate
  - BiPAP(Biphasic Positive Airway Pressure) or SiPAP(Synchronized Positive Airway Pressure)
  - Mechanical ventilation if drugs fail.

Self assessment quiz

Case 16

This is a 29 week baby is brought to the neonatal unit. He was born in good condition requiring minimal resuscitation and is put on to nasal CPAP in 25 % oxygen. Over the next four hours, his condition deteriorates. Oxygen requirement increases. There is obvious recession and he is having recurrent apneas. A capillary gas at this point shows mixed acidosis



a. **What is the most likely diagnosis?**
b. **What are the 3 appropriate actions you should consider?**
c. **What does his chest x ray show?**

Case 17

A 3-day-old, 790-g female infant had been ventilated for respiratory distress syndrome and was being weaned effectively from the ventilator. Today she is noted to have an active precordium, bounding pulses, and hypoxia with hypercarbia.

a. **What are the 2 most important investigations urgently needed?**
b. **What are the 3 most important differential diagnoses?**

Case 18

A term 3500-g female delivered by cesarean section develops a respiratory rate of 70 breaths/min and expiratory grunting at 1 hour of life. She has good tone, good color, and a strong suck.

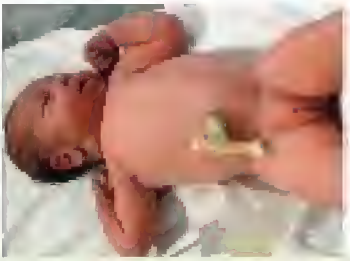
a. **What is the most likely diagnosis?**
b. **What are the 3 most important actions you should do?**

Case 19

A girl is born via cesarean section to a 34-year-old mother whose pregnancy was complicated by hypertension and abnormal fetal heart monitoring (cardiotocogram;CTG). At delivery she is covered in thick, green meconium and is limp, apneic, and bradycardic. **What is the appropriate action plan?**

Abnormal Gestational Age And Birth Weight

Definitions



- **Full term**: Infant born between 37-42 weeks gestations regardless to his weight

- **Premature** (pre term): Infant born < 37 weeks gestations regardless to his weight

- **Postmature** (post term): Infant born > 42 weeks gestations <u>regardless</u> to his weight

- Small for date (small for gestational age or intra uterine growth retardation):
  Infant with birth weight < 10th percentile of expected from his gestational age.
- Appropriate for date:
  Infant with birth weight between 10th and 90th percentile of expected from his gestational age.
- Large for date (Large for gestational age; macrosomia):
  Infant with birth weight > 90th percentile of expected from his gestational age.

Low Birth Weight infants (LBW)

- Any newborn with birth weight less than 2.5 Kg
- Includes:- Premature & Small for Gestational Age
- If birth weight < 1500 grams it is Very Low Birth Weight (VLBW)
- If birth weight < 1000 grams it is Extremely Low Birth Weight (ELBW)

Small for gestational age (SGA)

Alternative Names:

IUGR (Intra uterine growth restriction or Intra uterine growth retardation)

Infant with birth weight < 10th percentile of expected from his gestational age

Causes

Fetal causes	Maternal causes
– Onset usually in the 1st trimester – Usually symmetric IUGR ;weight, length and head are all <10th centile – Fetal anomalies common	– Onset usually in the 2nd -3rd trimester – Usually asymmetric IUGR (Head sparing) – Fetal anomalies less frequent
- Congenital infections. - Chromosomal disorders - Multiple congenital anomalies	- Maternal malnutrition and poor health - Placental insufficiency - Maternal smoking or drugs

Clinical Features

- Alert, active& hungry unlike the hypo activity of premature
- Good crying and suckling power
- Low weight (Head may appear large relative to the body)
- Loose, dry, scaling skinl with little subcutaneous fat
- Little muscle mass in the limbs and trunk
- Liable to intrauterine distress → Meconium staining

Complications

- Perinatal asphyxia
- Meconium aspiration
- Pulmonary hemorrhage
- Hypoglycemia, hypocalcemia and hypothermia
- Polycythemia and hyper bilirubinemia

Management

Antenatal (if IUGR suspected)

- Repeat fetal ultrasound assessments as often as 1-2 times per week
- Doppler blood flow studies (umbilical artery, umbilical vein, fetal aorta and cerebral arteries)
- Assessment of amniotic fluid volume (amniotic fluid index)
- Cardiotocogram (CTG) assessment; may be daily

Natal/Postnatal

1. Consider early delivery based on the above assessments and gestation
2. Consider antenatal steroids
3. Expert resuscitation as per neonatal life support guidelines
4. Neonatal care as before
5. Encourage Early and frequent feeding
6. Anticipate and manage hypoglycemia, hypocalcemia and polycythemia

Prematurity

Features of preterm baby

1. Clinical picture of preterm

- Birth weight: < 2.5kg (except infant of diabetic mother).
- Birth length: < 47 cm (except infant of diabetic mother).
- Head circumference: < 33cm.
- Chest circumference: < 30 cm.
- Scalp hair: fine and woolly.
- Skin:
  - Thin, pink, shiny, with little subcutaneous fat
  - Covered with lanugo hair(fine hair present on infants of 24 to 32 weeks' gestation).
- Nails: Don't reach the finger tips.

2. Physical appearance: help in assessing gestational age:

- Ear → shapeless and soft (immature ear cartilage).
- Breast nodule → < 3mm diameter (or even No breast tissue palpable).
- External genitalia → Female: prominent clitoris, labia majora widely separated, labia minora protruding
  → Male: scrotum smooth, no testes in scrotum
- Sole creases → don't reach beyond the anterior 2/3rd of sole (or even absent).

3. Physiological features

- Activity: Weak crying and activity, hypotonic with frog leg posture.
- Hearing
- Startles to loud noise
- Cry: Faint
- Sucking and swallowing: uncoordinated
- Physiological jaundice:
  - Delayed (after the 3rd day)
  - Prolonged (for 2weeks)
  - Deeper (up to 15 mg/dl).

4. Growth

- Preterm infants have rapid growth.
- Preterm infants at 28 weeks' gestation double their birth weight in 6 weeks and treble it in 12 weeks

Complications of prematurity

Respiratory

Problem	Etiology
○ Respiratory distress syndrome	– Surfactant deficiency
○ Apnea of prematurity	– Immature respiratory centre – Weak chest wall Pliable
○ Air leaks e.g. pneumthorax	– Positive pressure ventilation
○ Aspiration syndromes	– Hypoactive gag and cough reflexes
○ Bronchopulmonary dysplasia	– Prolonged oxygen therapy/ventilation

Cardiovascular

Problem	Etiology
○ Patent ductus arteriosus	– Fluid overload
○ Heart failure	– Fluid overload – PDA
○ Hypotension	– Impaired water and electrolytes regulation

Neurologic

Problem	Etiology
○ Kernicterus	– Immature blood brain barrier
○ Intraventricular hemorrhage	– Fragile ,pressure passive cerebral blood vessels – Fluctuations in blood pressure
○ Hypoxic-ischaemic encephalopathy	– Many risk factors
○ Retinopathy of prematurity	– See later
○ Sensineural deafness	– Late sequel to perinatal asphyxia

Hematologic

Problem	Etiology
○ Anemias	– Frequent sampling – Defective stores e.g. iron,folic,…
○ Coagulopathy /DIC	– Defective coagulation factors

Gastro intestinal

Problem	Etiology
○ NEC	– See before
○ Gastro oesphageal reflux disease(GORD)	– Weak cardia , ↓ gastric capacity and hyperactive pyloric muscles
○ Poor weight gain	– Poor suckling, swallowing and digestion and absorption

Nutritional

Problem	Etiology
○ Osteopenia of prematurity	– Phosphate deficiency
○ Rickets	– Vitamin D and calcium deficiency
○ Malnutrition	– High growth rate – Poor suckling, swallowing and digestion and absorption – Little subcutaneous fat

Renal

Problem	Etiology
○ More prone to – Dehydration – Metabolic acidosis	– Immature renal functions : - ↓ capacity of urine concentration - ↓ capacity of acid formation

Metabolic

Problem	Etiology
○ More prone to – Hypoglycemia – Jaundice	– Little glycogen stores – Immature hepatic enzymes

Immunologic

Problem	Etiology
○ More prone to – Neonatal sepsis – Neonatal meningitis	– Deficient humoral & cellular immunity – Decreased transplacental antibodies – Deficient physical barriers – Invasive techniques as exchange transfusion / catheterization / intubation

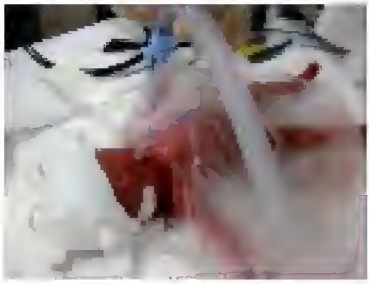
Temperature control

Problem	Etiology
○ Hypothermia	– Little subcutaneous fat – Immature heat regulating center – Large surface area relative to weight → excess heat loss

Management of prematurity/SGA

Prenatal management

- Induction of fetal lung maturity by prenatal steroids for VLBW and ELBW
- Consider prenatal transfer to a higher center



Delivery room management

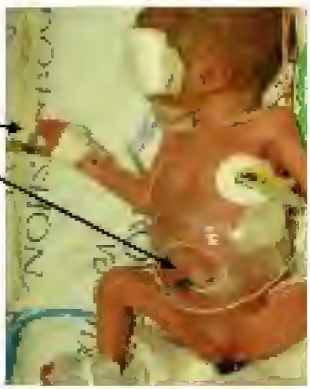
Resuscitation

- Resuscitate as usual very gently (see before)
- Keep dry and warm; plastic bags may be used
- Consider nasal CPAP very early
- Consider ET tube insertion if <28 weeks (oral distance = 6+ (wt in kg)
- Give surfactant if
  - Intubation was required in resuscitation
  - Preterm require > 40% oxygen to keep saturation >90% for 15-30 minutes

NICU management

Initial

- Venous access (UVC),and arterial line
- Start glucose infusion
- Give vitamin K 0.5 mg IM or IV
- Start empric antibiotics after cultures and swabs
- Respiratory support : Early CPAP, surfactant and respiratory monitoring
- Circulation support



Further care

1. **Thermoregulation and skin care**
2. **Fluids balance**

Amount

- On the 1st day of life, 60-80ml/kg (90 ml/kg if VLBW)
- Advance by 20 ml/kg per day to a maximum of 150-180 ml/kg per day.
- Adjust up and down according to the infant's clinical condition, plasma sodium, urine output(normal=1-3ml/kg/hour) and daily weight change

Type

- Dextrose 10% (or 5% in ELBW)
- Check electrolytes and calcium at 12-24 hours of age
- Electrolytes added after 24 hours of age, when urine output is adequate
- Basal needs are sodium is 2-3 mEq/kg/d, potassium 1-2 mEq/kg/d, and calcium 45 mg/kg/d (elemental calcium).

3. Nutrition

A. Total Parenteral Nutrition (TPN)

- I.V. administration of all nutrients (fats, carbohydrates, proteins, vitamins and minerals) necessary for metabolic requirements and growth while awaiting attainment of adequate enteral intake
- Given via peripheral vein, UVC or peripherally inserted central catheter(PICC)
- Calories
  - Start with 50 kal/kg/day
  - Increase slowly to 90-100 kal/kg/day by day 5 – 7 of life
  - Energy targets (*kcal/kg/day*):120 for premature , 140 for IUGR And 100 in term infants **(Concise pediatrics)**
- Macronutrients

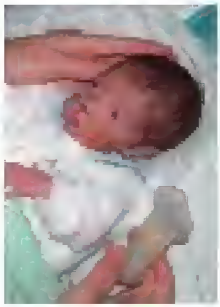
	Glucose	Protein	Lipid
Start	4-6 mg/kg/min	1 gm/kg/day	0.5 gm/kg/day
Start day	1st day	1st day	2nd day
Advance by	0.5-1 mg/kg/min	1 gm/kg/day	0.5 gm/kg/day
Maximum	12 mg/kg/min	3.5 gm/kg/day	3gm/kg/day
Monitoring	Blood glucose	Blood urea nitrogen	Serum triglycerides
Caloric share	50 %	10 %	40%
Preparation	D5% for <1kg D10% for >1 kg Concentrations > 12.5% ;use PICC	Aminovenous 10% (1 grams/10ml)	Intralipid 10% (1gram/10ml) Intralipid 20% (2gram/10ml)

- Micronutrients
  - Water soluble vitamins (Soluvit)
  - Lipid soluble vitamins (Vitalipid 4ml/kg/day added to intralipid)
  - Phosphate(Glycophos)
  - Trace elements

B. Enteral feeding

- Avoid in
  - Babies on pressors e.g. Dopamine
  - Hemodynamically significant PDA requiring indomethacin or ibuprofen or surgical closure
  - Sepsis/suspected sepsis
  - Abnormal GIT examination or large/green residuals

- Enteral feed choice
  - Mother's Breast milk plus fortifiers or premature formula
- Route
  - Nasogastric tube(NGT) until 35-36 weeks of age
  - Large preterm >35weeks can be fed by suckling



- Plan
  - Trophic feeding (minimal enteral feeding)
    - Started at 48 hours for 3 days
    - Amount: 1 mL q 2- 4 hrs.
    - Precautions:
      a) Feeds should be stopped only if there are signs of intolerance ; abdominal distension, significant vomiting, bilious aspirates or if NEC is suspected.
      b) Recommence after 4-6 hrs as symptoms resolve
  - Nutritional feeding
    - Started on day 5 or at 48 hours for stable babies > 1kg (When it is clear that minimal enteral feeds are tolerated)
    - Amount :1- 2mL q 3 hrs
    - Feeding advance: 1mL q 8 hrs

C. **Nutritional supplements** (mainly for those born at <34 wks gestation)

- Multivitamin drops
  - Started by 2 weeks of age (or at start of enteral feeds if later)
  - Orally, once daily for up to 1yr
  - Vitamin D 1000 IU/day, Folic acid 1 mg/day, Vit E 6-8 IU/day
- Iron
  - Begin by 2-4 weeks of life when enteral feedings are tolerated
  - Dose 2-4 mg elemental iron/kg/day until 6 months corrected age

4. Identify and treat complications e.g.

a. Episodes of apnea and bradycardia and desaturation

- Exclude an underlying cause.
- Caffeine citrate
- CPAP is often necessary

b. Intraventricular hemorrhage

- Usually occur within the first 72 hours of life
- Common in those with perinatal asphyxia and severe RDS
- Management (see before)

c. Patent Ductus Arteriosus (PDA)

- May be asymptomatic
- May cause
  - Apnea and bradycardia
  - Increased oxygen requirement
  - Difficulty in weaning the infant from artificial ventilation
  - Bounding pulse , basal systolic murmur and heart failure
  - Echocardiography is diagnostic
- Management (for symptomatic infant)
  - Avoided by careful fluid balance
  - Restrict current IV fluids
  - Pharmacologic closure with indomethacin or ibuprofen
  - Surgical ligation if pharmacologic closure fail

d. Retinopathy of prematurity (Retro-lental fibroplasia)

Definition

- Retinal vascular proliferation which may progress to retinal detachment, fibrosis and even blindness

Risk factors

- All babies < 1500 g birth weight or < 32 weeks' gestational age
- Exposed to uncontrolled high concentrations of oxygen (controversial)

Clinically

- No warning signs, so screening of babies at risk is mandatory
- Often gradually occurring astigmatism, retinal detachment , and amblyopia

Management

Preventive

- Screening of babies at risk is before discharge, and at 3 months of age
- Lowest O_2 for the least duration if O_2 therapy is indicated (controversial)

Curative

- Laser therapy
- Follow up the affected babies at 6 months intervals

e. Bronchopulmonary dysplasia (BPD) /Chronic Lung Disease

- Infants who are oxygen dependent at a post-menstrual age of 36 weeks
- Lung damage is due to pressure and volume trauma from artificial ventilation, oxygen toxicity and infection.
- Chest X-ray :shows widespread areas of opacification, sometimes with cystic changes
- These babies are more susceptible to recurrent wheezing, severe bronchiolitis and chest infections

f. Neurodevelopmental problems

High incidence of

- Cerebral palsy
- Delayed language development
- Sensorineural hearing loss and visual impairment.

Discharge from incubator

a. Criteria for discharge

- Infant > 1800 grams with good suckling.
- Adequate oral feeding (can tolerate 150 ml/kg per day)
- Maintain his temperature outside the incubator
- Normal vital data outside the incubator.
- No critical illness nor abnormal lab findings
- Infants with mild BPD may be discharged home on home oxygen therapy with nasal cannula

b. Make notes for

- Clinical examination with discharge weight and head circumference
- Discharge summary and discharge medications prescribed

c. Instructions to the parents:

- Keep infant away from infection ; minimize handling and over crowding
- Schedule for feeding
- Schedule follow up visits to monitor growth, feeding and neurodevelopment and vaccination (according to chronologic age)
- Advice given to parents regarding how and when to seek medical advice

d. Some babies require arrangements for:

- Hearing screening
- Screening for retinopathy of prematurity
- Hip ultrasound e.g. if family history of developmental hip dysplasia or breech delivery (usually done at 4 weeks of age)

Postmaturity

Definition

Infant born after 42 completed weeks of gestation, as calculated from the mother's last menstrual period, regardless of weight at birth

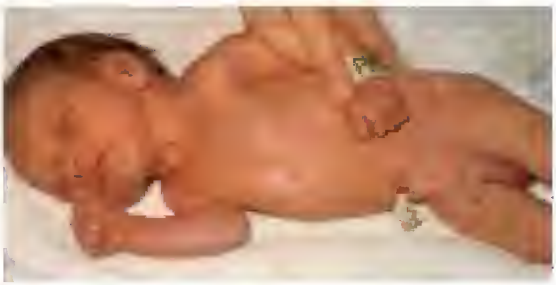
Causes

- Unknown in most cases.
- High incidence with trisomies or anencephaly.

Features

(Most features are due to placental insufficiency)

- Face : opened eye and alert baby
- Skin : pale,wrinkled, peeling, no lanugo hair ± meconium staining.
- Nails : long nails.
- Weight : average or decreased
- Normal length and head circumference



Complications

- Perinatal asphyxia ± Meconium aspiration syndrome
- Hypoglycaemia (depleted glycogen stores).
- Polycythaemia
- Hypocalcaemia.
- Persistent pulmonary hypertension

Prognosis

When delivery is delayed 3 wk or more beyond term, mortality is significantly increased; approximately 3 folds as for full term

Neonatal Hypoglycemia

Definition

- In neonates; there is no consensus about blood glucose level below which hypoglycemia is defined
- Practical definitions (not evidence based)
  - In the first 24 hours: blood glucose < 40 mg/dl (2.2 mmol/l)
  - Above 24 hours after birth: blood glucose < 45 mg/dl (2.5 mmol/l)
- WHO recommends keeping blood glucose > 47 mg/dl (2.6 mmol/l)

(Neonatal Emergencies, Harvard University, 2010)

Risk factors for hypoglycemia

1. **Increased demand or decreased supply**
   - Small for gestational age
   - Preterm
   - Perinatal asphyxia
   - Polycythemia
   - Hypothermia
   - Neonatal sepsis
2. **Hyperinsulinism e.g.**
   - Large for gestational age e.g. Infant of diabetic mother
   - Hemolytic disease of newborn
   - Beckwith Wiedemann syndrome
3. **Endocrinopathy**
   - Growth hormone deficiency
   - Congenital adrenal hyperplasia
4. **Inborn errors of metabolism**
   - Glycogen storage disease
   - Galactosemia
   - Organic academia
   - Fatty acid oxidation defects

Clinical Picture

1. Asymptomatic: common presentation
2. Symptomatic:

- Jitteriness	- Apneic episodes
- Tachypnea	- Lethargy or floppiness, poor feeding
- Pallor	- Cyanosis
- Weak or high-pitched cry	- Convulsions or eye-rolling

Management

Routine screening and monitoring of blood glucose is recommended only for infants who have risk factors or who have clinical manifestations

1. Asymptomatic high risk babies

- Keep warm
- Feed early (within 1 hour of birth) and if enteral feeding contraindicated start glucose 10% (D10%)infusion
- Glucose screening 30 minutes after the first feed
- If low despite feeding, give D10% bolus of 2-4 ml /kg IV
- Monitor blood glucose before 2nd,3rd ,4th feeds and until at least 2 consecutive normal blood glucose
- If the baby is already on IVF, ensure that glucose intake is appropriate

Glucose intake (mg/kg/min) = fluid rate (ml/hr) × % glucose / 6 × weight (kg)

- In term = 3-5 mg/kg/min
- In preterm = 4-6 mg/kg/min
- In SGA = 6-8 mg/kg/min

2. Symptomatic

- Immediate D10% bolus 2- 4ml/kg followed by continuous D10% IV infusion
- If hypoglycemia persists; ↑ glucose infusion rate steadily up to 10-12 mg/kg/min
- If hypoglycemia persists; add hydrocortisone 2.5 mg /kg 6hourly
- Monitor blood glucose frequently until stable

↓

A. Blood glucose stable ≥ 50 mg/dl for 24 hours

- Withdraw hydrocortisone slowly
- Taper the infusion gradually and advance feeding

B. Consider hyperinsulinism if glucose infusion rate ≥ 12 mg/kg/min

- Workup include: Hypoketotic hypoglycemia with increased c peptide
- Drug options: Glucagon ,Diazoxide, Somatostatin analogue

C. Persistent hypoglycemia

- Investigate for endocrinopathy
- Investigate for inborn errors of metabolism

N.B: - Blood glucose results <40 mg/dl should be confirmed in the laboratory
- Dextrose concentration > 12.5% should be given via a central venous line

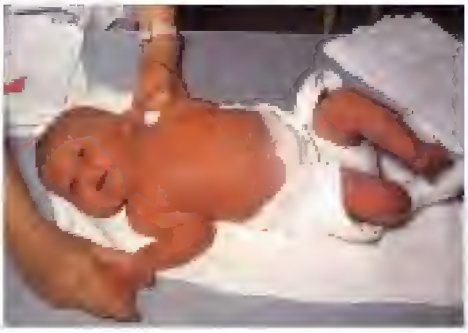
Infant of diabetic mother

Definition

- Neonate born to diabetic mother (Frank or gestational diabetes mellitus).

Features

- Commonly delivered preterm with ↑ birth weight (Large for gestational age)
- Plump with puffy plethoric facies



Why?

Maternal hyperglycemia → fetal hyperglycemia → increase fetal hepatic glucose uptake, glycogen synthesis & enhance lipogenesis & protein synthesis → macrosomia (increased growth of all organs except for the brain)

Common problems

2. Metabolic

- Hypoglycemia (in 25 %) due to: Maternal hyperglycemia → fetal hyperglycemia → increased fetal insulin production. After birth → interruption of high maternal glucose to the neonate while hyperinsulinemia is going on → hypoglycemia (usually marked after 1-3 hours postnatal)
- Hypocalcaemia & hypomagnesemia due to: transient hypoparathyroidism
- Hyperbilirunbinaemia due to: polycythaemia and reduced RBCs life span

(*Both hypoglycemia and hypocalcaemia →jitteriness and seizures*)

3. Respiratory

- Respiratory distress syndrome
- Transient tachypnea of newborn

4. Hyper insulinemic features

- Macrosomia may predispose to difficult labor & birth injury
- Transient hypertrophic cardiomyopathy
- Visceromegaly
- Polycythemia (Renal vein thrombosis is common)

4. Congenital anomalies (are 3 fold common, especially)

- Congenital heart diseases
- Sacral agenesis
- Left microcolon
- Neural tube defects

Management

* Proper control of maternal diabetes and follow guidelines for preterm delivery
* Natal and postnatal
  - Delivery room and NICU care
  - Treatment of hypoglycemia
    - Encourage early feeding
    - Monitor blood glucose before every feed
    - Manage hypoglycemia as before
  - Observe for and manage complications
    - Polycythemia (hydration , partial exchange)
    - Jaundice (phototherapy)
    - Echocardiography if heart murmurs or other signs suggesting congenital heart or cardiomyopathy
  - Discharge if no hypoglycemia for 24–48 hours on enteral feeds only and no other complication

Oesophageal atresia / Trachea Oesophageal Fistula

Definition

- Congenitally interrupted esophagus
- One or more fistulae may be present between the malformed esophagus and the trachea.

Clinical types

			
Type A (10%) Oesophageal atresia without fistula (pure esophageal atresia)	**Type B (< 1%)** Oesophageal atresia with proximal TOF	**Type C (85%)** Oesophageal atresia with distal TOF	**Type E (4%)** TOF without oesophageal atresia (H-type fistula)

Incidence

- 1:3500 live births
- More than half will have additional malformations

History

Antenatal ultrasound sometimes shows

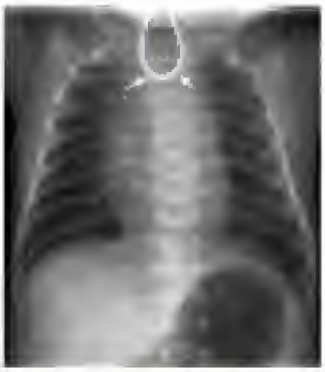
- Polyhydramnios
- Absent stomach bubble
- Associated congenital anomalies

Clinical features

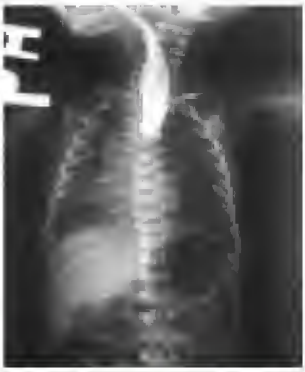
- Excessive production of frothy saliva
- Episodes of chocking and cyanosis exacerbated with attepts at feeding
- Failure to pass naso gastric tube

Investigations

- Chest x ray with naso gastric tube in situ reveals tip of tube in the oesophageal pouch ; presence of gas in stomach indicate a fistula
- Barium swallow can detect H type (avoided in atresia; risk of aspiration !!)
- Search for other anomalies by Echo , renal ultrasound ,spine x ray



Plain x ray chest shows curling up of the NGT in the oesophgeal pouch



Barium swallow shows barium filled esophageal pouch

Barium swallow shows H shaped TOF

Management

- Nurse head up and prone
- Pass a large bore tube and keep on low level suction to prevent aspiration of secretions
- Transfer to a surgical center when stable for repair

Duodenal atresia

Definition

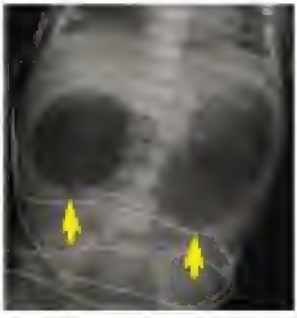
Congenital discontinuity of the duodenum usually in the region of the ampulla of Vater that leads to bowel obstruction

Incidence

Down syndrome (30%), prematurity and malrotation

Clinical features

- Antenatal history of polyhydrammios
- Bilious vomiting within hours of birth
- Distended stomach
- Delayed passage of and small amounts of meconium



Investigations

- Abdominal x ray :double bubble sign of distended
- stomach and duodenum
- Blood : electrolytes, glucose and blood gases

Treatment

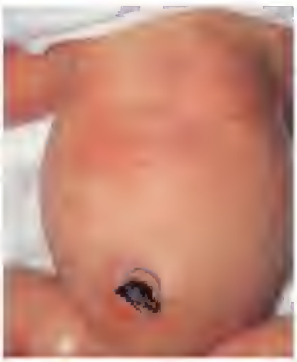
- Stop enteral feeding, start IVF, and insert nasogastric tube on free drainage
- Correct electrolyte and acid base disturbances
- Transfer to a surgical center when stable for repair

Benign Neonatal skin disorders

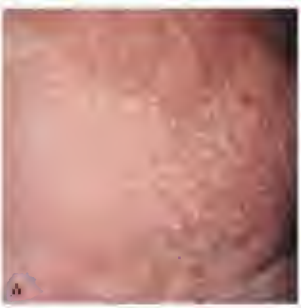
Criteria

- Etiology is unknown in most of them
- Require no treatment
- Fade spontaneously

1. **Erythema toxicum neonatorum**
   - Benign, self-limited, asymptomatic disorder
   - Lesions usually begin 24 to 48 hours after birth
   - Intense erythema with a central papule or pustule that resembles a flea bite
   - The eruption fades spontaneously within 5 to 7 days. No treatment is necessary



2. **Transient Neonatal Pustular Melanosis**
   - Presents at birth with 1- to 2-mm sterile vesiculopustules or ruptured pustules
   - Disappear in 24 to 48 hours, leaving pigmented macules with a collarette of scale



3. **Neonatal acne**
   - Multiple, 1- 2-cm ,yellowish-white papules
   - Usually located over the nose and cheeks of full-term infants
   - It represents a normal physiologic response to maternal androgenic stimulation of sebaceous gland growth

4. Cutis Marmorata

- Transient, netlike, reddish-blue mottling of the skin caused by variable vascular constriction and dilatation
- It is a normal response to chilling, and on rewarming, normal skin color returns

5. Mongolian spots

- Flat, slate-gray to bluish-black, poorly circumscribed macules.
- They are located most commonly over the lumbosacral area and buttocks
- More in dark skinned infants

Diaper Dermatitis

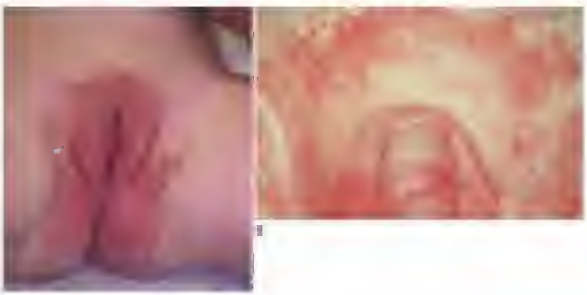
1. Irritant Diaper Dermatitis

- The diaper area is bathed in urine and stool and occluded by plastic diaper covers
- Failure to change diapers frequently provides time for fecal bacteria to form ammonia by splitting the urea in urine
- Erythema; scaling; and, at times, maceration are usually confined to the convex surfaces of the perineum, lower abdomen, buttocks, and proximal thighs, sparing intertriginous areas

Treatment

- Frequent diaper changes and gentle cleansing
- Lubricants and barrier pastes
- A short course of low-potency steroids may hasten resolution

2. Candidal Diaper Dermatitis



- A common sequela of oral or parenteral antibiotic therapy
- Bright red eruption, with sharp borders and pinpoint satellite papules and pustules
- Intertriginous areas are involved
- May be with oral thrush

Treatment

- Topical antifungal therapy
- The occasional resistant case may require a brief course of oral medication.

3. Staphylococcal Diaper Dermatitis

- Thin-walled pustules on an erythematous base
- Typically, these rupture rapidly and dry, producing a collarette of scaling around the denuded red base

Treatment

- Oral and topical antibiotics

Examination of newborn

Quick examination

Value: detect life threatening insults

- Apgar scoring ⇒ (done at 1, 5 minutes; at 5 minutes is more important).
- Normal newborn is conscious, active, alert
- Color
  - Normal newborn is pinkish in color.
  - Abnormal appearance of the newborn may be:
    - Pallor
    - Plethora
    - Cyanosis
    - Jaundice
- Vital signs
  - Heart rate (120 – 140 beat/minute)
    - < 80 → Bradycardia
    - > 180 → tachycardia
  - Respiratory rate (≈ 40 /minute)
    - > 60 → tachypnea (RD)
  - Temperature (36 – 37.5°C)
    - < 35.5 → hypothermia
  - Mean blood pressure (should equal gestational age in weeks)
- After the end of quick examination the newborn will be considered as
  - Normal → Proceed to other lines of examination.
  - Abnormal → Admit e.g. to NICU

Detailed examination

Measurements

- Weight
- Length
- Head circumference

Regional examination

a- Head

- Anomalies / dysmorphism
- Birth trauma
- Fontanels

- Congenital cataract /subconjunctival hemorrhage
- Oral moniliasis

b- Neck

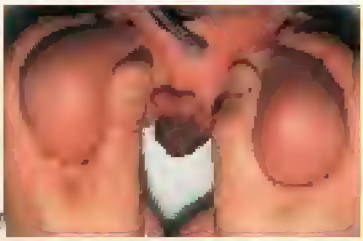
- Short neck or webbing (Turner).
- Goitre (enlarged thyroid).

c- Limbs

- Birth trauma /Malformations.
- Developmental Hip Dysplasia (DDH)

Risk factors

- Family history
- Breech presentation
- Oligohydramnios
- Congenital myopathies and neurological disease



Screening

- If risk factor present and newborn examination is normal
- Hip ultrasound scan at 4-6 weeks
- Refer to orthopedics only if ultrasound abnormal

Abnormal clinical examination include

- Positive Ortolani s test (Abducting the femur produces a palpable clunk)
- Positive Barlow s test (femoral head pushed more away from acetabulum)
- Asymmetrical gluteal creases
- Limited hip abduction
- Unequal leg length

If hip examination confirmed to be abnormal

- Arrange for early hip ultrasound (Between 2- 4 weeks of life)
- Arrange early orthopedic referral

d- Genitalia

- Ambiguous genitalia
- Undescended testis/ Hypospadius

e- Skin

- Meconium staining skin , nails and umbilical stump
- Edema (Hydrops fetalis).

f- Urine and stool

- Normal neonate should pass urine & meconium within 24 hrs of birth

Systemic examination

a- Cardiovascular system

- Apex beat: Normally in Left 4th space at the mid clavicular line.
- Murmurs: Most of murmurs in early neonatal period are transient
- Femoral pulsations: If absent Aortic coarctation is suspected.

b- Chest examination

- Signs of respiratory distress.
- Apnea.
- Auscultation for wheezes, crepitations, …..

c- Abdominal examination

- Liver may be palpable 2 cm in neonates
- Check for organomegaly, ascitis, umbilicus, …..
- Causes of neonatal abdominal masses e.g.:
  - Hydronephrosis.
  - Multicystic – dysplastic kidney.
  - Ovarian cyst.
  - Intestinal duplication.
  - Neuroblastoma.
  - Wilm's tumor.
- Scaphoid abdomen with severe respiratory distress strongly suspect congenital diaphragmatic hernia

d- Neurological examination

- Level consciousness.
- Muscle tone (normally flexed all limbs).
- Neonatal reflexes.(tendon reflexes and primitive reflexes)

Special examination

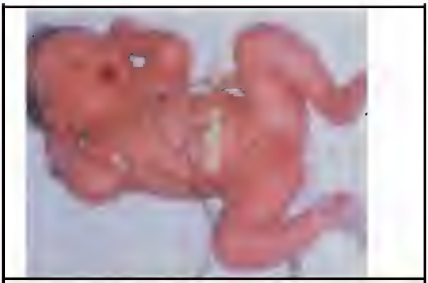
1. Check for congenital anomalies e.g.
   - Cleft lip
   - Tracheo-esophageal fistula
   - Limb anomalies e.g. talipes equinus
   - Congenital heart diseases
   - Imperforate anus.
2. Search of birth injuries e.g.
   - Cranial injuries
   - Nerve injuries
3. Assessment of gestational age
   - From the history (last menstrual period).
   - From the ultrasound exam. during pregnancy
     - Biparietal diameter
     - Femoral length
   - From physical and neurological assessment: New Ballard Score

The New Ballard Score

- A set of procedures developed by Dr. Jeanne L Ballard, to determine gestational Age through neuromuscular and physical assessment of a newborn fetus
- Usually done after newborn stabilization

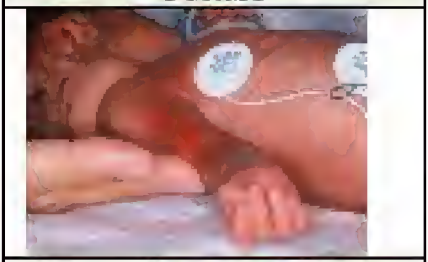
A. Neuromuscular maturity

Score	-1	0	1	2	3	4	5	Sign score
Posture								
Square window (wrist)	> 90°	90	60	45°	30	0°		
Arm recoil		180°	140–180°	110–140°	90–110°	< 90°		
Popliteal angle	180°	160°	140°	120°	100°	90°	< 90°	
Scarf sign								
Heal to ear								

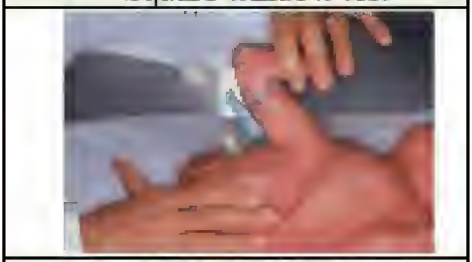


Posture

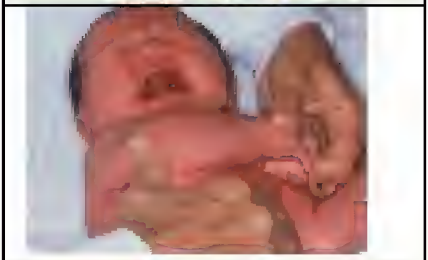
Square window test



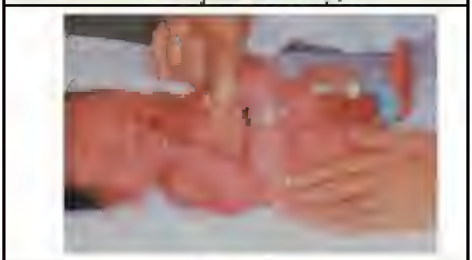
Arm recoil



Popliteal angle



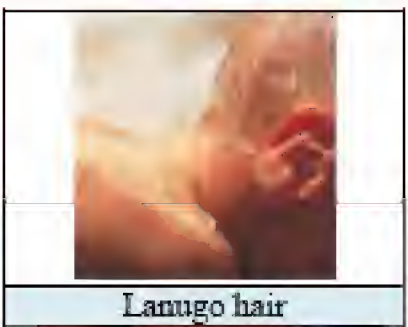
Scarf sign

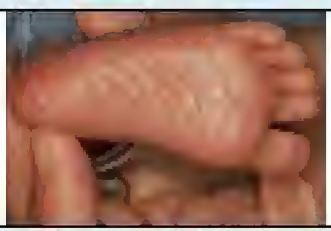


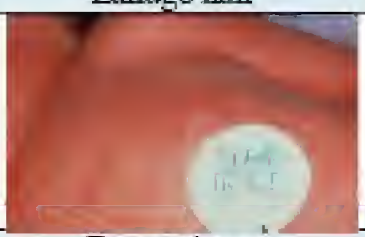
Heal to ear

B. Physical maturity

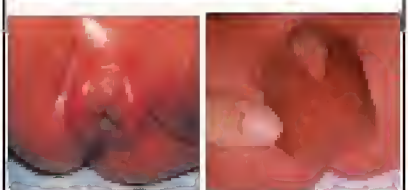
Sign	Score							Sign score
	-1	0	1	2	3	4	5	
skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth pink, visible veins	Superficial peeling &/or few veins	Cracking, pale areas, rare veins	Parchment, deep cracking, no vessels	Leathery, cracked, wrinkled	
Lanugo	none	Sparse	Abundant	Thinning	bald areas	mostly bald		
Plantar surface	Heel-toe 1:40- 50 mm 2: < 40 mm	> 50 mm no crease	Faint red marks	Anterior transverse crease only	Creases ant. 2/3	Creases over entire sole		
Breast	Imperceptible	Barely perceptible	Flat areola no bud	Stippled areola 1-2 mm bud	Raised areola 3-4 mm bud	Full areola 5-10 mm bud		
Eye /ear	Lids fused 1: loosely 2: tightly	Lids open pinna flat stays folded	Curved pinna; soft, slow recoil	Well-curved pinna; soft but ready recoil	Formed & firm instant recoil	Thick cartilage ear stiff		
Genitals Male	Scrotum flat, Smooth	Scrotum empty, faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae		
Genital Female	Clitoris prominent & labia flat	Prominent clitoris & small labia minora	Prominent clitoris & enlarging minora	Majora & minora equally prominent	Majora large, minora small	Majora cover clitoris & minora		
							Total physical maturity score	


Lanugo hair


Plantar surface


Breast tissue


Ear pinna


Genitalia

Total score	Weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

تم بحمد الله

دكتور/ محمد الكومى

استاذ مساعد طب الاطفال وحديثى الولادة بكلية الطب- جامعة الزقازيق

زميل الكلية الملكية لطب الاطفال – لندن

زميل المستشفى الملكى للاطفال(كوين اليزابيث) - جلاسجو- اسكتلندا

Facebook: Mohamed Elkouni

Email:mohamed_197228@hotmail.com

Mobile number:+201000089045

Answers

Growth and development

Case 1

a. Absent both tibial and femoral epiphysis (i.e. delayed bone age)
b. Congenital hypothyroidism
c. Widely open anterior fontanel and open posterior fontanel > 1 cm

Case 2

D

In congenital adrenal hyperplasia, a deficiency of enzyme 21-hydroxylase causes an interruption in the pathway for production of cortisol; the end result is hypersecretion of androgenic precursors and clinical manifestations of virilism and protein anabolism and there is rapid growth in stature, with marked acceleration of osseous maturation. The result is early closure of epiphyses and failure to achieve full growth

Case 3

B

A normal 3-month-old infant can raise his or her face 45° to 90° from the horizontal. Not until 6 to 8 months of age should an infant be able to maintain a seated position

Case 4

C

Infant feeding

Case 1

a. lactose intolerance secondary to post gastro enteritis syndrome
Clinical pointers to diagnosis:
- Persistent diarrhea
- Peri anal soreness
- Irritability with distended abdomen

b. Laboratory diagnosis
- Detect reducing substance in stool (lactose)
- Detect acidic pH of stool (lactic acid)

c. Use of lactose free milk for two weeks

Case 2

a. A humanized formula
b. Feed at 3 hours intervals, so number of feeds about 8/24 hours
c. Amount of milk required /feed
- Age in months X 10 ÷ 100 = 120 ml
- Amount can be calculated by caloric method as well

d. Preparation of the formula (concentration of milk given)

i- Formula of dried powdered milks:

- One measure of 4 gm diluted by 30 mL boiled water e.g. Liptomil, Nan, Aptamil 1.
- One measure of 8 gm diluted by 60 mL boiled water e.g. Similac, S 26.

ii- Formula of fresh fluid animal milk: not preferred at all before 1 year

Case 3

a. Cow milk protein allergy

b. Laboratory test required

- Occult blood in stool
- A Skin prick test or radioallergosorbent test (RAST)
- Therapeutic trial of milk withdrawal is more informative

c. Use of Casein hydrolysate based formula; the best choice

N.B

- Most gastrointestinal manifestations resolve within several days
- Cow's milk in the mother's diet is the most common identifiable cause of food-allergic reactions in nursing infants
- About 50% of infants who experience proctocolitis while nursing improves with removal of cow's milk from the mother's diet

(*Nelson textbook of pediatrics*)

Case 4

1. Lactose free formula
2. Predigested formula
3. Phenylalanine low formula
4. Lactose free formula
5. Premature formula

Nutrition

Case 1

a. Probable diagnosis; Edematous PCM (mostly Kwashiorkor)

Features suggesting diagnosis:

- Characteristic edema
- Muscle wasting
- Weight /expected weight at 10 months between 60-80% with edema
- Skin changes over buttocks
- Pallor; indicating possible anemia
- Enlarged liver

b. see textbook

Case 2

a. Dietetic Marasmus

b. Possible 4 risk factors

- Exclusive breast-feeding and delayed weaning
- Insufficient breast milk
- Being one of twin; usually have higher growth rates
- Low birth weight

Case 3

a. 3rd degree marasmus secondary to congenital heart disease; ASD

b. Congenital heart disease; ASD

c. Direct your investigations to diagnose the congenital heart disease e.g. echocardiography ,chest x ray and ECG

d. Lines of treatment

- Consult pediatric cardiologist and nutritionist
- Medical
  - Control heart failure (diuretrics, digoxin, vasodilaters).
  - Dietetic treatment as before
- Interventional/Surgical
  - ASD complicated with growth failure will usually require transcatheter or open heart surgical closure when the baby reaches suitable size for intervention

Case 4

a. Rickets complicated with hypocalcemia tetany

b. See treatment of tetany

Case 5

B

Case 6

E

Genetics

Case 1

a. Turner syndrome
b. See textbook

Case 2

a. Down syndrome
b. Duodenal atresia and congenital acyanotic heart disease (likely endocardial cushion defect or VSD)
c. Place a nasogastric tube and start IV fluids and electrolytes
   Treatment of the congenital heart disease
   Investigate for and treat jaundice
   Surgical consult for a duodenostomy.
d. An echocardiogram
   A karyotype

Case3

Subluxation of the atlantoaxial joint

Case4

- Likely diagnosis is Down syndrome complicated by acute leukemia (acute myeloid leukemia or acute lymphoblastic leukemia)
- Immediate blood film with differential count for blast cells and arrange for bone marrow examination at the first chance

Diarrhea

Case 1

a. **Diagnosis:** Intussusception complicating acute gastro enteritis

b. **Investigations:**

Abdominal ultrasound is the gold standard to diagnose Intussusception

Other important investigations:

- Serum electrolytes
- Blood urea nitrogen and creatinine
- Stool culture
- CBC

c. **Management:**

Correct dehydration and electrolyte disturbances

Consult pediatric surgeon immediately

Case 2

a. Severe dehydration

b. Insert IV line →Take blood sample for investigations (Electrolytes /BUN/ CBC/ Blood gases) →Push 20 ml /kg normal saline IV and watch for improvement of perfusion and mental status

Case 3

a. Moderate (to severe) dehydration

b. ORS is not suitable due to repeated vomiting and being tired

c. Amount of fluids required = 100 ml /kg

Infection

Case 1

a. Pertussis (baby was infected most likely from his mother)

b. Confirm diagnosis by nasopharyngeal swab and smear or PCR or culture for B. Pertussis and B. Para pertussis

Case 2

Typhoid fever

Case 3

a. Typhoid fever

b. The important 4 lines of treatment including
   - Keep NPO, Intravenous line and intravenous fluids (correct shock then maintenance fluids)
   - Fresh blood transfusion
   - Ceftriaxone IV daily
   - Surgical consultation for possible resection of involved part (Don't forget typhoid fever is a notifiable disease)

Case 4

a. Neonatal tetanus (tetanus neonatorum)

b. Picture (a) shows Risus Sardonicus and trismus (lock jaw) and photo(b) shows tonic or board like rigidity and Opisthotonus

Case 5

If a child is unimmunized, or immunization is incomplete for tetanus, a dose of the appropriate vaccine for age should be given, along with tetanus immune globulin (TIG) if the wound is considered dirty. As this child is 5 years old, DTaP would be the best choice according to the childhood immunization schedule.

Case 6

- Intramuscular immune serum globulin can prevent measles if given within 6 days of exposure
- Live vaccination is given 3 months later

Case 7

a. Rubella

b. Measures for her mum include: test immediately for Rubella antibodies
   - Negative and remain negative means she escaped infection
   - Positive for Rubella Ab IgG means she is immune
   - Negative and turn up positive means she got the infection

(If the mother got the infection; abortion is much better than IVIG)

Case 8

a. Important 4 investigations include:
   - Viral markers to exclude other causes of hepatitis ; HBV,HAV,HCV,CMV
   - Heterophile antibody tests to confirm infectious mononucleosis
   - Sepsis screen :Blood culture, throat swab
   - Prothrombin time assesses severity of hepatitis

b. Diagnosis: Infectious mononucleosis with EBV hepatitis

Case 9

a. Erythema infectiosum
b. Parvo B19 virus

Case 10

a. Varicella
b. Varicella associated cerebellitis and cerebellar ataxia
c. Clinical recovery is typically rapid, occurring within 24-72 hr, and is usually complete without treatment

Case 11

a. Hand Foot and Mouth disease
b. Coxachie A virus

Case 12

a. Mumps complicated with minengoencephalitis and orchitis
b. CT scan brain and ,when hemodynamically stabilized, lumbar puncture
c. Lumbar puncture likely shows evidence of viral meningitis
   - Increased pressure of cerebrospinal fluid
   - Increased protein
   - Normal sugar
   - Dominance of lymphocytes in the cell population
   - No bacteria

Case 13

a. Mumps complicated with acute pancreatitis and viral myocarditis
b. Investigations are
   - For myocarditis : chest x ray (cardiomegaly), ECG, and Echocardiography
   - For acute pancreatitis: serum lipase, serum calcium, lipid profile, abdominal ultrasound and CT

Neonatology

Case 1

a. Apgar score at 1 minute 3

b. Apgar score before 5 minutes 10 (crying baby = Apgar score 8-10)

Case 2

a. Immediate first actions include:

- Dry and wrap
- Open airway
- Call for help
- Assess breathing, HR, color and tone

b. Next steps include

- Inflation breaths 5 at 30 cmH_2O for 2-3 seconds each to see chest rise
- Ventilation breaths;15 breaths over 30 seconds
- External cardiac massage for 30 seconds
- Reassess as before

c. Next actions

- Insert endotracheal tube
- Continue ventilation and cardiac compressions

d. Send blood for pH, blood gases, hemoglobin and glucose

e. Adrenaline 0.1 ml/kg 1:10.000 solution

f. Repeat adrenaline and give sodium bicarbonate and request for emergency O negative blood transfusion

g. Continue care and mechanical ventilation in NICU

Case 3

a. Fluoroscopy of the chest

b. Phrenic nerve palsy associated with Erb's palsy

Case 4

Fracture of right clavicle

Case 5

a. Adrenal hemorrhage (difficult breech delivery ,and possible asphyxia at birth are risk factors in addition to bleeding tendency with prolonged PT,PTT)

b. Emergency abdominal ultrasonography

c. Initial 4 lines of treatment after securing ABC:

- Fresh blood transfusion and follow up of hemoglobin
- Fresh plasma transfusion and follow up of PT and PTT
- Vitamin k therapy

- Phototherapy and follow up of TSB

Case 6

a. Neonatal sepsis suggested by:
   1. Risk factors: Premature Rupture of membranes 21 hours, Maternal intrapartum fever 38.1C
   2. Not doing well neonate pale and mottled respiratory distress and lethargy

b. Chest x ray shows nonspecific coarse opacities of both lung fields more on the right (in the course of sepsis ;neonatal pneumonia is suggested)

c. Sepsis screen (discuss) ,blood glucose , electrolytes and blood gases

Case 7

a. There is Pneumatosis-intestinalis and thickened intestinal wall

b. NEC

c. Hold enteral feeds, NGT, start TPN→ obtain sepsis workup → empiric antibiotics→ surgical consult (see treatment for NEC)

Case 8

a. Congenital rubella syndrome

b. Blueberry muffin rash (see CRS): this rash is not pathognomonic to CRS ;it can be seen in congenital CMV infection and severe hemolytic disease of newborn

Case 9

a. Physiologic jaundice exaggerated with the cephalhematoma

b. Only phototherapy is required

Case 10

a. ABO incompatibility

b. Investigations
   - Reticulocytic count (RC)
   - Direct coombs test
   - Blood film
   - Serial assessment of Hb% ,TSB and RC

Case 11

a. Breast milk jaundice

b. Hold breast milk for 24-48 hours and feed formula milk(*now optional*)

(N.B: If there is no response and TSB continues to rise ,Crigglar Najjar syndrome should be considered and a therapeutic trial with oral phenobarbitone should be instituted)

Case 12

a. Diagnosis
   - Acute bilirubin encephalopathy(kernicterus)
   - Secondary to hemolytic disease of newborn due to ABO incompatibility
   - Risk is increased by the cephalhematoma

b. Investigations
   - Direct Coombs test
   - Serial follow up of TSB and Hb%
   - For the cephalhematoma:
     - Skull CT
     - Brain ultrasound

     (To rule out intracranial hemorrhage as a cause of seizures)
   - Sepsis workup (to rule out sepsis as a cause of not doing well newborn)

c. Management
   - Immediate exchange transfusion
   - Extensive phototherapy during waiting for and after exchange
   - Serial follow up of TSB and Hb%
   - IVIG

Case 13

a. The most likely diagnosis is hemorrhagic disease of newborn due to vitamin K deficiency

b. The 3 most important lines of treatment
   - Parenteral vitamin K
   - Fresh plasma transfusion
   - Fresh blood transfusion

Case 14

a. Swallowed maternal blood

b. Apt test for the bloody stool

Case 15

a. Severe perinatal asphyxia

b. Clinical (via Sarnat grading), Neuro imaging and EEG

Case 16

a. Respiratory distress syndrome

b. The 3 appropriate actions
   - Intubate, ventilate and give surfactant
   - Request chest x ray
   - Give antibiotics after sepsis workup

c. Severe RDS , white lungs

Case 17

a. Obtain a chest film and obtain an echocardiogram
b. PDA, pneumothorax and endotracheal tube obstruction if intubated

Case 18

a. Transient tachypnea of newborn
b. The 3 important actions:
   - Provide supplemental oxygen as needed
   - Request sepsis workup (blood and chest x ray)
   - Initiate empiric antibiotics combinations till cultures come back negative

Case 19

See your text book